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EDITORIAL

THE LABORS OF SISYPHUS

"With many a weary step and many a groan,
Up a high hill he rolls a huge round stone;
The huge round stone, revolting with a bound,
Thunders impetuous and smokes along the ground."

LIKE THESE ETERNAL LABORS are those of the officials who have charge of the enforcement of laws relating to the food and drug supplies of the several nations and the subdivision thereof, state, municipal, and so forth. One fraud may be suppressed, but another and sometimes more than one may arise to replace it. A recent issue of this journal contained some data about many cosmetics and fat-reducers ascertained by the State Board of Health of New Hampshire. There is just at hand a report of the U. S. Department of Agriculture which gives facts regarding more than one thousand preparations advertised as antiseptics. These include mouth-washes, douche powders, suppositories, salves, liniments, dusting powders, tooth pastes, and soaps.

Few manufacturers had ever tested their products bacteriologically. Some were under the impression that a chemical such as carbolic acid would be antiseptic no matter how weak the solution. Hundreds of preparations were found misbranded and bearing false claims.

The most an antiseptic can be expected to do is destroy or inhibit the growth of bacteria on or very close to body surfaces. Many of these misbranded preparations were found to be offered as competent treatments for abscesses, grippe, hemorrhoids, sores of every description, sore throat, all forms of skin diseases, and some serious visceral diseases. Some were even recommended to be taken internally for indigestion, stomach ulcers, cholera morbus and dysentery.

Most of the mouth-washes and douche powders were found to be modifications of preparations described in the National Formulary as

"antiseptic solution" and "antiseptic powder." The first of these is antiseptic only when used full strength; the second only when used as a dry dressing but not when dissolved in water for use in douching.

When manufacturers were advised to label their products truthfully to avoid violating the Federal Food and Drugs Act, the majority willingly and promptly either revised their labels and directions or changed their formulas to justify the claims made. Makers of forty-five so-called antiseptics removed their preparations from the market rather than make any changes or face legal action. In only twenty cases was it necessary for the administration to resort to legal action to secure compliance with the act.

The drive against worthless and misbranded antiseptics for human and animal use resulted from representations made late in 1926 to the Department of Agriculture that many antiseptics were being sold in open violation of the Federal Food and Drugs Act, which requires that all drug products sold in interstate trade be correctly and truthfully labeled.

In a preliminary survey of several well-known antiseptics, it was found that most of these were either non-antiseptic or recommended in dilutions too weak to have any effect. In fact, two of the so-called antiseptics examined at that time actually contained living bacteria.

The need of making a nation-wide survey of all antiseptic preparations became evident to protect the public from fraud as well as from the consequences of placing confidence in useless medicinal products. The first public announcement of the drive was made at the April 7, 1927, meeting of the American Drug Manufacturers Association by two Department of Agriculture officials. Definitions of the word "antiseptic" as found in correct dictionaries were discussed.

It was pointed out at that time, and it has been the unchanging stand of the administration ever since, that the important factor in deciding whether an antiseptic should kill bacteria or simply prevent their growth is the length of time the product would be in contact with the body. Such products as mouth washes, douches and gargles, as used, are in contact with the body for but a few seconds, and therefore can only be considered antiseptic if they kill bacteria in the dilutions recommended and in the length of time they are in contact with the body. Salves, ointments, dressings and other products in contact with the body for prolonged periods of time may properly be called antiseptic if they merely prevent the growth of bacteria.

Concerning this matter, it must be borne in mind that the Federal authorities can control only the articles entering into interstate commerce. Goods sold exclusively within a given state can only be controlled by the laws and health authorities of that State.

HENRY LEFFMANN.

SELECTED EDITORIALS

THE CORNER DRUG STORE AND MODERN CIVILIZATION*

THIS IS PHARMACY WEEK and recognition is due to the men and women who seem to work all the time behind counters and partitions in the service of a mostly unappreciative public.

The drug store is an American institution. All druggists are philosophers, sometimes of the misanthropic school—and small wonder. O. Henry began life as a drug clerk, and he took the trade into his later work. Other men of leadership have begun the same way. A pharmacist must know everything, from the highly skilled compounding of a vital prescription to the best brand of lipstick. He must have a marvelous memory, or the names of all the proprietary medicines he sells would not be on the tip of his tongue. He knows all the neighborhood gossip, and mostly keeps it to himself. In a small town he is a figure of influence, known to all. His title of "Doc" he wears becomingly.

Drug stores have figured in national life. The Scopes evolution case, that had the world standing on its head for awhile, started in one. Behind more than one prescription partition vast political schemes have been hatched. Lincoln did not disdain to foregather with cronies behind one in Springfield. Soda fountains today dominate the beverage industry and "soda jerkers" run off with rich widows.

Physicians respect and depend on pharmacists as fellow practitioners. They must work together, and they do. The proprietor of a drug store is also, as well, a father confessor. He is all the time asked to prescribe for minor ailments, and when there is a street accident he is called on to provide first aid.

*From the *Newark Evening News.*

Pharmacists handle deadly drugs every day; how seldom they make a mistake! Pharmacy is an exact science; in the nature of things it must be. Prescription experts seldom are seen, but they exert a tremendous influence over life and death.

Drop in to see your druggist this week. He is a good fellow.

ORIGINAL ARTICLES

ILLICIUM RELIGIOSUM, SIEBOLD*

Mang Tsao

A PHYTOCHEMICAL STUDY

By Sze Yee Chen

(*Continued from the August Issue*)

Estimation of tannin.[2] 250 cc. of an aqueous solution were made from 20.00 grams of the ethereal extract. Two 100 cc. samples were taken, diluted to 130 cc. each and treated with 10 grams of hide powder. The results obtained are herewith tabulated:

	Dist. water	*Aq. sol. 0*	*Aq. sol. 1*	*Aq. sol. 2*
Amount used	100 cc.	50 cc.	100 cc.	100 cc.
Ether ext. equivalent	8.0 g.	4.0 g.	8.0 g.	8.0 g.
Amt. of water added	30 cc.	15 cc.	30 cc.	30 cc.
Hide powder	10.0 g.	10.0 g.	10.0 g.	10.0 g.
Amt. of detann. sol. taken for evaporation	10 cc.	10 cc.	10 cc.	10 cc.
Residue	0.0190 g.	0.3471 g.	0.2640 g.	0.2636 g.
Correction			0.0190 g.	0.0190 g.
Correc. wt. of residue		0.3471 g.	0.2450 g.	0.2446 g.
Tannin absorb			0.1021 g.	0.1025 g.
Average			0.1023 g.	
Tannin content			16.03 p.c.	

*Thesis submitted for the degree of Doctor of Philosophy, University of Wisconsin, 1927.

[2] Procter, *Principles of Leather Manuf.*, 2d ed. (1922), p. 349; Rosenthaler, *Grundzuege d. chem. Pflanzenuntersuch.* 1923, p. 71; Schmidt, *Pharm. Chem.* II (1911), p. 1476.

Estimation of Reducing Substances

By means of Fehling's solution and Molish's test it was found that the aqueous solution made from the ethereal extract contains some reducing substance. Quantitative estimation was, therefore, made using Benedict's method. The solutions prepared for the tannin determinations were used with the following results:

	Orig. sol.[1] *(not dilute) (not detann.)*	*Detan-*[2] *nized solution*	*Detan. sol.*[3] *Boiled for 40 min.*	*Detan. sol. Boiled with 1 p.c. H_2SO_4 40 min.*
cc. of Benedict's sol. taken	5.00[4]	5.00	5.00	5.00
Solution for titration	2.70	3.15	15.00	11.55
" " "	2.70	3.05		
Average	2.70	3.10	15.00	11.55
g. of equivalent ethereal ext.	0.216	0.1908	0.1846	0.1422
p.c. of reducing sugar calculated as glucose	4.63	5.23	5.40	7.03

The higher content of reducing sugar in the detanninized solution than in the original solution may be due to the loss of solvent in the detannizing process with the dry hide powder. The tannin was removed by treating 100 cc. of the solution with 10 grams of hide powder in a closed flask for 14 hours and then filtering. The filtrate thus obtained was assumed to have the same strength in reducing power as the original solution.

Isolation of protocatechuic acid. Eykman[1] has isolated protocatechuic acid from the ethereal solution of *Illicium religiosum* by extracting this solution with caustic alkalies, acidifying the alkaline

[1] Benedict, *J. Am. Med. Assoc.*, 57, 1193 (1911); Hawk, *Practical Physiological Chem.* 7th ed., 1921, p. 530, Mathews, *Physiol. Chem.* 3d ed., 1923, p. 1119.

[2] This solution was prepared by diluting 5.0 cc. of the detanninized solution water and boiling, making the final solution up to 25 cc.

[3] This solution was prepared by diluting 5.0 cc. of the detanninized solution to 30 cc. with water, adding 3.0 cc. H_2SO_4 (6N) boiling for 40 min. neutralizing with $BaCO_3$, filtering off excess of $BaCO_3$ and bringing the resulted sol. up to 25 cc.

[4] 5.00 cc. of Benedict's solution equivalent 10 mg. of glucose.

[1] *Recuil d. Trav. Chim. des Pays-bas* 4 (1885), p. 32.

extract with mineral acid, taking up the free acid with ether, and purifying by recrystallization from hot water. Oswald [2] repeated the same experiment with success. In my experiment the ether-soluble portion was taken and shaken repeatedly with 10 p.c. $NaHCO_3$ solution until the ethereal solution gave no more effervescence. The $NaHCO_3$ extract was then treated slowly with diluted HCl (if a concentrated acid was added quickly to the alkaline solution the latter became warm and an aromatic odor developed, thus indicating the decomposition of some substance in the solution), and the free acid thus liberated was taken up with ether. The ether was removed by spontaneous evaporation and the residue was dissolved in hot water, treated with charcoal, boiled for an hour, and filtered while hot. Upon spontaneous evaporation of the aqueous solution needles resulted in rather impure form which melted at 193°. Protocatechuic acid melts at 198°. The lowest melting point of this acid has been reported at 194°.[3]

Attempts to isolate the toxic principle. It has been definitely shown by Eykman,[1] Langgaard,[2] Honda,[3] and K. K. Chen [4] that the toxic principle of *Illicium religiosum* is very readily soluble in chloroform and alcohol and insoluble in petroleum ether. Since in the experiments here recorded the chloroform-soluble portion obtained from the alcoholic extract which had previously been washed with heptane and ether, was much less toxic than the ether-soluble portion, the latter was used.

After the removal of the protocatechuic acid by means of sodium bicarbonate solution, the ethereal portion which had been mixed with a large amount of water was acidified with acetic acid and the resinous material thus separated was filtered off. The aqueous filtrate which contained only a very small amount of ether was neutralized with ammonium hydroxide and shaken with chloroform. On evaporation of the chloroform there was left an impure residue which was again dissolved in hot water and extracted with the same solvent. Upon evaporation a yellow residue of thick consistency was obtained. Part of this material was soluble in ether. Both the ether-soluble and insoluble portions were found to be highly toxic to rats.

[2] *Archiv der Pharm.* 229 (1891), p. 84.
[3] Barth and Schmidt, *B.* 12 (1879), p. 1265.
[1] *Pharm. Jour.* 40 (1880-1881), p. 1046.
[2] *Virchow's Archiv* 86 (1881), p. 222.
[3] *Arch. d. Pharm.* 52 (1905), VI, p. 83.
[4] *Loc. cit.*

As K. K. Chen has stated that the treatment with ammonia destroys the toxicity, another portion of the ethereal extract was dried, powdered and triturated with boiling water. The residue was filtered off and the filtrate repeatedly extracted with chloroform. After the removal of the chloroform, the residue was again separated into an ether-soluble portion and an ether-insoluble portion. The former was green and melted at 150–160° while the latter was yellowish and melted between 50–60°. Both portions were tested for alkaloid but with negative results.

Direct extraction of the powdered drug with chloroform. 150 grams of the material were percolated with chloroform until exhausted. Most of the solvent was distilled off and the insoluble matter which separated on cooling was removed by filtration. The filtrate was diluted with a large volume of petroleum ether and the residue treated with ether. The ether-insoluble portion was fairly soluble in chloroform but was thrown out of the solution by the addition of petroleum ether as a white powder which became a brownish, sticky mass on the removal of the solvent and exposure to the air. Most of the ether-soluble material was soluble in sodium hydroxide.

Second lot of Illicium religiosum. Since the amounts of some constituents, more particularly the fatty acids, the non-saponifiable matter, the volatile oil and the toxic principle were too small to permit of satisfactory investigation, a second lot of *Illicium religiosum* was ordered and received from Peking. Since this was treated in a somewhat different way the procedure is herewith described.

Extraction with alcohol. 17.5 kg. of finely powdered fruit were exhausted with alcohol in a Lloyd extractor. After removal of the alcohol from the percolate, the concentrated extract (6.82 kg. or = 39 p.c. of the crude drug) was percolated with acetone until the readily soluble material had practically all been removed. 3.12 kg. (=18.0 p.c.) of solid substance were left in the percolator, consisting mainly of shikimic acid. The acetone-soluble portion, which amounted to 3.48 kg., was first distilled to recover the solvent and the residue extracted successively with benzene, chloroform, and ethyl acetate. Four different portions were thus obtained.

1. Benzene-soluble portion,	751 g.	(=4.3 p.c.),	S. V.= ——
2. Chloroform-sol. "	99 g.	(=0.57 "),	S. V.= 368
3. Ethyl acetate-sol. "	85 g.	(=0.49 "),	S. V.= 329
4. Insoluble residue	2510 g.	(=14.3 "),	S. V.= 226
			A. V.= 58.4

Steam distillation of the benzene-soluble portion. After removal of the solvent, the benzene-soluble portion was subjected to steam distillation, thus separating it into a volatile part, a fatty oil and an aqueous residue. The distillate which came over first consisted largely of benzene. It was, therefore, collected separately, and upon fractional distillation, 12 g. of volatile oil were recovered therefrom. This oil was kept separate. The total oil obtained from the later distillate and upon cohobation of the aqueous distillate amounted to 42 g. (=0.31 p.c. of the crude drug). This part of the oil was used for the determination of the physical as well as the chemical constants.

The volatile oil. The volatile oil had a spicy odor and a yellow color which on standing turned deeper. The following constants were determined: $\alpha_{24}{}^{\circ} = 0.9884$; $\alpha_D = -4.52^{\circ}$ in 100 mm. tube; $n_{26}{}^{\circ} = 1.050$; A. V. = 0.35; S. V. = 43.7. It did not congeal in a freezing mixture at -8°.

The aqueous residue from steam distillation. 3 liters of aqueous residue were obtained after the steam distillation of the volatile oil. The aqueous solution was separated from the fatty oil by means of a funnel, and freed from traces of greasy matter by filtration. This large volume was reduced by evaporation on a water bath and then in a vacuum desiccator over sulphuric acid. The resulting residue consisted of a syrup with a bitter as well as a sweetish taste. It reduced Fehling's solution rapidly, and gave a positive reaction with Molish's test.

About 0.2 cc. of this syrup were heated with a mixture of phenylhydrazine hydrochloride and sodium acetate in boiling water for thirty minutes. No crystalline compound was formed. But on cooling some impure precipitate appeared.

Chloroform-soluble portion. The chloroform-soluble portion was deprived of the solvent by distillation and of traces of oily matter and chlorophyll by washing with benzene. The fairly thick residue was then shaken vigorously four times with boiling water. The aqueous solution thus obtained was filtered through a double filter in order to remove traces of greasy and coloring matter. It was then distilled under reduced pressure on a water bath. The temperature did not rise above 35°. The water which distilled over had an acid reaction as indicated by methyl red, while the concentrated aqueous solution had a syrupy consistency, a brownish color and a bitter taste. It reduced Fehling's solution readily and gave positive reaction with Molish's test. Thirty minutes heating with phenylhy-

drazine hydrochloride and sodium acetate did not give a crystalline compound or precipitate.

Saponification of fatty oil. 430 grams of fatty oil which had a saponification value of 205.4 were boiled with 130 g. of potassium hydroxide in one liter of alcohol for one hour on a water bath. The alcohol was removed by distillation under reduced pressure. The residue was dissolved in hot water and the aqueous solution, after cooling extracted with ether until almost all the yellowish coloring material had been removed. From the ethereal solution 68 grams of non-saponifiable matter were obtained. From the aqueous solution the organic acids were liberated by the addition of 1 :1 hydrochloric acid. They were washed with water until the washings were neutral to litmus paper.

Separation of solid and liquid fatty acids by means of lead-salt-ether method. The free organic acids were neutralized with aqueous potash using phenolphthalein as indicator. To the soap solution, kept at boiling temperature and constantly stirred, a hot solution of 300 grams of lead acetate in 1½ liters of water was added. The lead soap was washed with water, dried under reduced pressure and extracted with ether. Treatment of the ether-soluble and -insoluble lead soaps with 1 :1 hydrochloric acid under ether yielded 108 grams of liquid fatty acid and 178 grams of solid fatty acid, respectively.

Examination of solid fatty acids. Melissic acid. The total solid fatty acids, 178 grams, were dissolved in 800 cc. of 99 p.c. alcohol and kept in an ice box over night. 1.2 grams of fine precipitate were obtained. After treatment with charcoal in 95 p.c. alcohol and recrystallization from the same solvent it was perfectly white and melted at 88.5° to 90°. Melissic acid from beeswax melts at 88.5°,[1] that from myricyl alcohol is reported to melt at 88.5° to 89.0° [2] and 90° to 91°.[3]

After being dried at 55° under 30 mm. pressure for four hours the acid value was determined.

Sample	(1)	0.1123 g.	A. V.	124.6
	(2)	0.1382 g.	A. V.	129.3
		Average		126.9

The A. V. calculated for $C_{30}H_{60}O_2$ is 124.1.

[1] Rigg, *Ann.* 235, p. 235.

[2] Sahwalb, *Arch d. Pharm.* 246, p. 172.

[3] *Jour. Am. Chem. Soc.*, 41 (1919), p. 75.

The phenacyl ester of this acid was prepared according to Rather's method [4] except that the potassium salt resulting in the determination of the acid value, was used. It melted at 79.5°.

The same ester was made from bromoacetophenone and melissic acid prepared from wax. It melted at 81°.

Preparation of melissic acid from beeswax. Following Nafzger's method,[5] 100 grams of white wax were boiled repeatedly with 95 p.c. alcohol until the alcohol dissolved no more cerotin. The alcohol-insoluble portion which contained the myricin as ester was saponified with an excess of alcoholic potassium hydroxide. The alcohol was distilled off and the dried soap extracted with petroleum ether. The petroleum ether solution was washed with concentrated hydrochloric acid to remove any basic substance and then with water to free it from the mineral acid. After the removal of the solvent, the petroleum ether extract was repeatedly crystallized from 95 p.c. alcohol. A perfectly white substance, myricyl alcohol, melting at 88.5° was obtained. The melting point of myricyl alcohol has been reported as 85° by Brodie,[6] and as 88° by Gascard.[7] The latter has been recognized as the correct m.p.[8]

The petroleum ether-insoluble potassium salt was treated with warm concentrated hydrochloric acid and the acid liberated, washed four times with boiling water and then repeatedly crystallized from alcohol. It melted at 90°.

Stearic acid. The filtrate from the melissic acid was diluted with 20 cc. of water so to make a 95 p.c. alcoholic solution, and cooled in an ice box over night. 1.5 g. of precipitate were obtained. After purification by means of charcoal and crystallization twice from alcohol of the same strength it melted at 60–61°. Stearic acid melts at 69.3°. Its acid value was found as follows:

Sample	(1)	0.1677 g.	A. V.	197.6
	(2)	0.1878 g.	A. V.	199.8
		Average		198.7

[4] Stueke, *Ann.*, 223, p. 295.

[5] *Ann.* 224, p. 251.

[6] *Ann.* 71, p. 147.

[7] *Jour. Pharm. Chem.*, 1893, p. 49 (Lewkowitsch, *Chem. Tech. & Anal. of Oils, Fats and Waxes,* 6th ed. i, p. 246).

[8] Beilstein, *Handb.*, 1918, 1, p. 432.

A. V. for stearic acid is 197.6. Although the acid value of this acid agrees with that of stearic acid the melting point is rather low. It is, therefore, probably a mixture of melissic acid and some lower member acid.

Bulir [9] records the presence of 22.5 p.c. of palmitic and 2.5 p.c. of stearic acid in the total acid from the fatty oil of *Illicium religiosum.*

Daturic acid. To the filtrate from the stearic acid 25 cc. of water were added thus making a 90 p.c. alcoholic solution. After having been kept at 0° for 24 hours this solution yielded 5 grams of precipitate. This precipitate was treated with charcoal and recrystallized from 90 p.c. alcohol. The perfectly white substance melted at 57° and after recrystallization at 58°. The acid value was found as follows:

Sample (1)	0.0971	g.	A. V.	208.7
(2)	0.1241	g.	A. V.	205.4
	Average			207.1

The A. V. calculated for $C_{17}H_{34}O_2$ is 207.7.

As the melting point and acid value indicate it to be either a mixture of equal parts of stearic and palmitic acid (m.p. 56.6°[10] or daturic acid (m.p. 57°, or 59° see below), an attempt was made to effect a separation. Following Kreis and Hafner's method,[11] 2 grams of the acid mixture were dissolved in 200 cc. of 95 p.c. alcohol and placed in an ice box over night. Assuming it to be a mixture of equal parts of palmitic and stearic acid, all the palmitic acid and 0.12 g. of stearic acid should be in solution and 0.88 g. of stearic acid should be precipitated. But the experiment yielded only 0.131 g. as the insoluble part and this melted at 78° instead of in the neighborhood of 69° at which stearic acid melts. Hence this is probably a mixture of some melissic acid and a lower member acid. To the filtrate 0.301 gram of magnesium acetate dissolved in alcohol was added. After having been kept at zero temperature for 30 hours the solution became turbid and was filtered. The acid in the solution was liberated by the addition of water and crystallized from alcohol. It amounted to 1.6 grams and melted at 58°. This acid was treated once more

[9] *Zeitschr. f. Untersuch. d. Nahrgs. u. Genuss.* 24 (1912), p. 310.
[10] Heintz, *Ann.,* 92, p. 295 (Lewkowitsch, *Chem. Tech.,* 6th ed. 1, p. 120).
[11] *Ber.* 36, p. 2769.

with magnesium acetate and 1.3 g. were recovered. It melted at 58°. The acid value was found as follows:

Sample	(1)	0.1007 g.	A. V.	204.7
	(2)	0.1219 g.	A. V.	203.1
		Average		203.9

The acid value calculated for $C_{17}H_{33}COOH$ is 207.7.

Kreis and Hafner found that after one treatment with magnesium acetate the palmitic acid portion melted at 60° and after repeating this process once more pure palmitic acid melting at 62.3° was obtained.

The filtrate from which the acid was recrystallized was diluted with water. An acid melting at 58° was obtained.

Heptadecyclic acid or margaric acid synthesized by Krafft [12] melted at 59.3°. Meyer and Eckert [13] found an acid $C_{17}H_{34}O_2$ melting at 57° in coffeeberry oil. It had an A. V. of 203.1. Since this acid could not be separated into palmitic and stearic acid by means of fractional precipitation with lithium acetate they assumed it to be daturic acid. Noerdlinger [14] claimed the occurrence of daturic acid in palm oil. It melted at 57° and could not be separated into palmitic and stearic acids by means of fractional precipitation with magnesium acetate. Daturic acid gets its name from Datura from the oil of which it was first isolated by Gerard.[15] The phenacyl ester was made from the potassium salt and bromoacetophenone following the direction of Rather. It melted at 56° The same ester made from a mixture of equal parts of palmitic and stearic acid (Kaulbaum products) melted at 60°. The phenacyl ester of pure palmitic acid melts at 56° and that of stearic acid at 64°.

Palmitic acid. To the filtrate from which daturic acid had been precipitated 120 cc. of water were added to make a 75 p.c. alcoholic solution. After 24 hours in an ice box the precipitate was filtered off. It melted at 58–60°. Treatment with charcoal and repeated crystallization from alcohol increased the melting point to 61.5°. Palmitic acid melts at 62.9°. The acid value was found to be:

[12] *Ber.* 12, p. 1672.
[13] *Monatsch. f. Chem.* 31 (1910), p. 1238.
[14] *Zeitschr. f. angew. Chem.* 1892, p. 110.
[15] *Compt. rend.* 111 (1890), p. 305.

Sample	(1)	0.1003 g.	A. V.	211.8
	(2)	0.1819 g.	A. V.	210.7
		Average		211.3

Palmitic acid has an A. V. 219.0.

Residue after the removal of palmitic acid. After the removal of the palmitic acid the filtrate was again diluted with water until a 60 p.c. alcoholic solution was obtained. An oily material separated out, which on cooling in an ice box crystallized, but liquified when brought to room temperature. It was found to contain some liquid fatty acid.

Bromination of liquid acid. The mixture of liquid acids was brominated in ether-acetic acid solution using Farnsteiner's method.[16] No traces of hexabromide were found. The ethereal solution was next washed with a saturated solution of $Na_2S_2O_3$, then with water and finally dried over anhydrous Na_2SO_4. The ether was distilled off and the residue treated with petroleum ether. The precipitate was purified by dissolving in warm benzene, filtering through charcoal and recrystallizing from the same solvent. It melted at 113.5° The tetrabromide of linoleic acid melts at 114°.

Since it has been shown previously that the bromine content of this compound agrees fairly well with the theoretical value it was not redetermined. For the same reason the dibromide in the mother liquid was not investigated.

Non-Saponifiable Matter

Myricyl alcohol and a hydrocarbon. The reddish-brown non-saponifiable matter (65 grams) was dissolved in 500 cc. of warm alcohol and the solution cooled in an ice box over night. Three grams of soft white crystals separated out. By treatment with petroleum ether these crystals were resolved into a soluble and an insoluble part and both parts were recrystallized from 95 p.c. alcohol. The petroleum ether-insoluble part melted at 80–82°, and its acetate melted at 71°. Myricyl alcohol from beeswax melts at 85° as found by Brodie[1] and at 88° by Gascard.[2] Its acetate melts at 73°, 70° having also been recorded.[3]

[16] *Zeitschr. f. Untersuch. d. Nahrungs. u. Genussm.* 2 (1899), p. 1.
[1] *Ann.*, 71, p. 147.
[2] *Jour. de Pharm. et Chim.* 1893, p. 49.
[3] Lewkowitsch, *Laboratory Companion to Fats and Oils Industries,* 1901, p. 33.

From the fat of rice bran, Nabenhauer and Anderson [4] have recently isolated myricyl alcohol which melted at 80° in the impure condition and at 85° after several recrystallizations. The presence of melissic acid in the fatty oil and of myricyl alcohol in the non-saponifiable matter may throw some light upon the genetic relationship between the two. Whether they are present as an ester as in beeswax remains to be seen.

The petroleum ether-soluble portion had a paraffin-like appearance and a m.p. of 70–72°. The amount was too small for further purification or identification. From the non-saponifiable matter of rice bran Weihage [5] isolated a hydrocarbon $C_{27}H_{48}$ which melted at 79.5–80.5°. He believed that this hydrocarbon is closely related to phytosterol which it is similar to or identical with β-cholesterol.[6] α-Cholestan [7] $C_{27}H_{48}$ prepared from α-cholesterol melts at 72°. The petroleum ether-soluble part may, therefore, be assumed to be similar to or identical with α-cholestan.

Sitosterol. The combined mother liquids from recrystallization of the myricyl alcohol and the hydrocarbon were reduced to an alcoholic strength of about 70 p.c. when practically all the soluble material separated out. The precipitate had a melting point of 121–126°. After recrystallization from alcohol it was obtained as beautiful shining crystals melting at 134°. It gave a positive Salkowski-Liebermann reaction.[8] Its acetate was prepared using the directions given in Lewkowitsch's *Chem. Anal. of Fats, Oils and Waxes,* vol. 1, p. 598, and had a melting point of 122°. Sitosterol melts at 135–139°, and its acetate melts at 125°.[9]

Steam distillation of the alcohol-soluble portion. The aromatic odor of the nonsaponifiable matter suggested the presence of some volatile constituents. The solvent of the alcoholic mother liquid from which the myricyl alcohol, hydrocarbon and sitosterol had been removed was distilled off and into the residue steam was passed. After 7 liters of distillate had been collected practically no more volatile oil came over and the distillation was discontinued. Twenty grams

[4] *Jour. Am. Chem. Soc.,* 48 (1926), p. 2972.
[5] *Zeitschr. Physiol. Chem.* 100 (1917), p. 159.
[6] Diels and Linn, *Ber.* 41 (1908), p. 548.
[7] *Ibidem,* p. 547.
[8] *Zeitschr. f. physiol. Chem.,* 57 (1908), p. 515.
[9] Lewkowitsch, *Chem. Tech. and Anal. of Oils, Fats and Waxes,* 6th ed., I, p. 282.

of volatile oil were thus obtained. By extraction with ether 6.5 grams more were recovered from the aqueous solution. The physical constants of the oils were found as following:

	Original oil	*Ether-extracted oil*
d24°	1.0547	1.0486
n_D at 24°	1.4692	1.5253
Rotation in 100 mm. tube at 24°	−0.75°	−2.77°
Congealing pt. below	−10°	−10°

Fractional distillation of the volatile oil. The two portions of the volatile oil were united and distilled under diminished pressure. The following fractions were obtained:

Fraction	*Pressure*	*Temperature*	*Amount*	d22°	n_D
I	16 mm.	127–246°	1.5 g.		
II	15 mm.	147–149°	9.5 g.	1.0721	1.5240
III	15 mm.	150–154°	8.0 g.		
IV	15 mm.	157–192°	4.5 g.		
Residue		abt.	1. g.		
Loss			2 g.		
Total			26.0 g.		

Examination of the volatile oil from the non-saponifiable matter. The fractions had an aromatic odor like safrol. With the exception of the first fraction the light yellow color turned red on standing.

The characteristic odor, the great density and high boiling point suggested either safrol or isosafrol or a mixture thereof. Eykman[1] had found that the oil distilled directly from the fruit of *Illicium religiosum* contained safrol as the chief constituent. The presence of safrol in the non-saponifiable matter is, therefore, not improbable. In the process of saponification of the fatty oil from which the non-saponifiable matter was obtained, the safrol might have been changed to iso-safrol. For comparison the constants of both safrol and isosafrol are herewith tabulated:

[1] *Rec. Trav.*, 4 (1885), p. 34.

	Safrol	*Iso-safrol*
$d15^{\circ}$ [2]	1.096, 1.107	1.124, 1.129
n_D [2]	1.536–1.542	1.580
b.p.[2 3 4]	93° at 5 mm.	107.5° at 5 mm.
	107° at 10 mm.	149° at 20 mm.
	123° at 20 mm.	253–254° at ordinary pressure
	233° at 759 mm.	
Rotation	Inactive	Inactive
Congealing pt.	–8°, –10° (2)	Does not congeal at –18°

The high boiling point and the low congealing point of the oil indicated it to be iso-safrol rather than safrol. In order to ascertain its identity the picrate was prepared according to Brun and Tornanis.[5] When an equivalent amount of the ethereal solutions of picric acid and of the oil were mixed and the mixture was allowed to evaporate spontaneously a red oil with some crystals was formed. A few of the crystals were separated and dried on a porous plate. They lost their red color and left a yellow crystalline powder which melted at 120°. Evidently this is picric acid which melts at 122°.

The remaining mixture of the red oil and the crystals was, therefore, heated in an oven at 60° for one hour. On cooling a red mass with needles was formed. The odor of the oil had disappeared. It melted at 78°, and the color turned greenish-black on keeping. Bruni and Tornanis reported that the picrate of iso-safrol consists of red, shining, stable needles melting at 73°.

Bromination of the oil. Following the direction of Hoering and Paul,[6] to 13 g. of bromine, cooled in an ice mixture, 1 g. of the fraction II (b.p. 147–149°) was gradually dropped in. At the end of the reaction the excess of bromine was distilled off on a water bath and residue washed with petroleum ether and then twice recrystallized from alcohol. A reddish, amorphous compound was obtained. It melted at 150–155°. The small amount available did not permit further purification. It was found to contain 51.6 p.c. of bromine. The

[2] G. H. K., *The Volatile Oils,* 1, p. 485.

[3] Semmler, *Die aether, Oele,* vol. 1, p. 149.

[4] Rechenberg, *Gewinn. u. Trenn. d. aether. Oele,* p. 510.

[5] *Atti R. Accd. d. 1 Roma* (5), 13, II, 1904, p. 84; *Centralb.* 75 (1904), II, p. 954.

[6] *Ber.* 40 (1905), p. 1101.

dibrom derivative of iso-safrol contains 49.6 p.c. of bromine, while the pentabromide, which was expected, has a bromine content of 71.2 p.c. The dibrom derivative has been reported as an oil, the tribromide to melt at 110° and the pentabromide at 195–197°.[7]

Phytosterols. The residue after steam distillation formed a semi-solid cake. It was dissolved in hot methyl alcohol. On cooling, white leaflets with a shining lustre crystallized out melting at 138°. Its acetate melted at 124–124.5°. Concentration of the mother liquid yielded another crop of crystals melting at 142° and the acetate melted at 92° (impure). According to Boemer [1] phytosterol melts at 137° to 138° and the acetate at 138° to 143.8° according to the purity of the preparation.

From the non-saponifiable matter of corn oil Schriner [2] isolated sitosterol melting at 141–142° and dihydrositosterol melting at 143–144°. Anderson [3] found that the hydrosterol in plant fats melts at 141–142° when impure and at 145–146° when in a purer condition. Its acetate according to Anderson melts at 137–141°.

Toxic Principle

The toxicity of *Illicium religiosum* or Japanese star anise has long been known in China and Japan. A chemical investigation was first made by Geerts [1] in 1880 who reported that the fatty oil was poisonous. His findings, however, were shortly afterward disproved by Eykman [2] who found that the fatty oil extracted from the seeds with petroleum ether was not poisonous. From the marc he isolated a crystalline body which he called shikimin and claimed it to be the chief toxic principle. It is a nitrogen-free substance melting at 175° and soluble slightly in water. In the same year (1881) Langgaard [3] examined the whole plant and concluded that the poisonous principle was extractable by cold water, not precipitated from the aqueous solution by lead acetate, not destroyed by hydrogen sulphide and by evaporation on water bath. All parts of the plant—the fruit, seed,

[7] Semmler, *Die aether. Oele,* IV, p. 149.

[1] Lewkowitsch, *Chem. Anal. of Oils, Fats and Waxes,* 6th ed. 1, p. 281.

[2] *Jour. Am. Chem. Soc.* 48 (1926), p. 2976.

[3] *Jour. biol. Chem.*, 71, p. 389.

[1] *Nieuw Tigdschrift voor Pharm.*, 1880, p. 298-312; *Jahrsb. u. die Fortsch. d. Pharmacog. Pharmacie u. Toxicol.*, 1880, 50; *Pharm Weekb.*, 17, #15.

[2] *Mitteil. Deutsch. Gesell. f. Natur- und Voelkerkunde d. Ost.* 22, Yokohoma, 1881; *Pharm. Jour.* 40 (1880), pp. 1046-50.

[3] *Virchow's Archiv.* 86 (1881), p. 222.

bark, wood, root and the leaf—are poisonous, the seed being the most toxic. The star anise acts in the same manner but in much smaller degree. The isolation of toxic principle from the air dried leaves was first accomplished by Honda [4] in 1905. The shikimiamine he obtained was a nitrogenous body melting at 175.5° and having the empirical formula $C_{32}H_{29}N_3O_9$. It is soluble in alcohol and chloroform and slightly soluble in cold water. Guirrero [5] records that the fruit of *Illicium religiosum* is fourteen times as toxic as that of *Illicium anisatum*. In 1919 Negrete and Velarde [6] found that the toxic principle is absorbed by animal charcoal and that the half-hour cold infusion and the half-hour decoction made on water bath representing equal amounts of the drug are equally toxic while 24 hours' maceration at room temperature produces a less toxic preparation. Chen [7] obtained the toxic principle as a resinous mass which refused attempts made to crystallize it. The latest investigation is that of Chou.[8] By repeated precipitation with different solvents he obtained from the seeds a white amorphous powder which is named shikimitoxin by him. The shikimitoxin sinters at 63° and liquidifies at 116°. It is soluble in chloroform, alcohol, less so in ether and hot benzene and insoluble in petroleum ether. The M.L.D. for cat is 0.2 mg. From this brief review it is evident that nothing very definitely is as yet known about the toxic principle of *Illicium religiosum.*

Isolation of toxic principle from the seeds. 155 grams of the seed were powdered and extracted in a Soxhlet apparatus with chloroform for two days. The marc was removed and repowdered and again extracted with the same solvent for two days more when the extract did not leave any residue on evaporation. The solvent was distilled off and the residue which amounted to 46 g. or about 30 p.c. was repeatedly shaken with water in a separating funnel. After the removal of the traces of oil material by means of filtration the aqueous solution was repeatedly extracted with chloroform until the extract was no longer colored yellow. The chloroform extract was then treated with double its volume of petroleum ether. After standing for two hours the clear liquid was decanted off and the resinous, reddish residue

[4] *Archiv. f. exper. Pathol. u. Pharmakologie* 52 (1905), pp. 83-94.
[5] *Philippine Jour. Sc.* 11 B, 203 (Sep. 1916).
[6] *Semana Med. Buenosaires* 26 (1919), pt. 2, pp. 554-565.
[7] *J. A. Ph. A.* 15 (1926), p. 861.
[8] *Chinese Jour. of Physiology* 1, #2, pp. 213-18.

amounted to 0.3 g. The residue was taken up with hot benzene leaving a large part insoluble. The benzene solution was again precipitated with petroleum ether, the precipitate extracted with water, the aqueous solution shaken with chloroform, the chloroform solution treated with petroleum ether, the precipitate treated with ether and the ethereal solution finally precipitated with petroleum ether. The precipitate thus obtained was still colored a light brown, but the amount was too small for further purification. It melted at 65–70°. It is highly toxic to white rat.

Toxic principle from the whole fruit. For this purpose the chloroform-soluble fraction (see extraction with alcohol of the second batch of *Illicium religiosum*) was used. This fraction was obtained from the whole fruit by extracting the powder (17.5 kg.) with alcohol. After the removal of the solvent the alcoholic residue was washed with acetone, and the solvent was again removed. The acetone residue was freed from the oil and coloring material by washing with benzene and then reflexed with chloroform on a water bath. After distilling off the chloroform a thick liquid was left which amounted to 99 g. The chloroform-soluble fraction thus obtained was triturated four times with hot water. The aqueous extract was filtered and concentrated under diminished pressure at a temperature not over 40°. The concentrated solution was repeatedly extracted with chloroform. The chloroform solution was precipitated with petroleum ether. The precipitate was taken up with hot benzene and to the cooled solution petroleum ether was added. The brownish precipitate was again treated with water and the aqueous solution extracted with chloroform. The chloroform was evaporated and the residue taken up with ether. The petroleum ether precipitate from this solution consisted of a gelatinous mass with a light yellow color. It was dried over P_2O_5 in a vacuum desiccator resulting in a solid which could not be powdered. Treatment once more with anhydrous ether left some impurities undissolved. This impurity which is brownish-yellow melted at 90–100° and was found highly toxic. From the ethereal solution a yellowish precipitate was obtained by the addition of petroleum ether. It melted at 60–65° and was highly toxic to white rat: 0.1 mg. killed a rat of 250 g. in 60 minutes. The toxic principle can be easily precipitated from any solution by heptane.

(*To be concluded in the October issue*)

PHYTOMICROCHEMICAL TESTS AS PHARMACOPŒIAL IDENTITY TESTS

By E. H. Wirth and J. A. Dorjahn

THE MICROCHEMICAL characterization of vegetable drugs is by no means new. Several books covering the general microchemistry of plants have been published, notable among which are "Pflanzenmikrochemie" by Tunmann and "Mikrochemie der Pflanze" by Molisch. Nevertheless the microchemistry of drugs has been, as a whole, generally omitted from drug descriptions both in textbooks and in pharmacopœias. This general omission is perhaps due to the fact that among the host of results described in the literature many do not lend themselves to successful reproduction, some are complex and some involve too great a technical skill to be carried out successfully by the average worker. There are however, many which are relatively simple and reliable. Some of these we desire to discuss.

Wirth[1] has pointed out the importance of microchemical tests demonstrating the active constituents of drugs in pharmacognostical laboratory instruction. The student who is able to remove from a few milligrams of the drug, crystalline substances which he can see, and upon which he can perform microchemical reactions surely obtains a better knowledge of that drug than he who considers only its morphology and anatomy. As Rosenthaler [2] has said, "there can be no doubt that microchemical characterization of drugs should not receive less consideration than the morphological-anatomical test, in as much as we use them (the drugs) on account of their active constituents."

In the pharmacognosy course of the School of Pharmacy of the University of Illinois each student is equipped with a kit of apparatus for such work [3] and many microchemical demonstrations of constituents in crude drugs are carried out by the student himself as a regular part of the course. As new tests appear in the availale literature

[1] *Jour. A. Ph. A.*, 17 (1928), 691-698.
[2] *Am. Jour. Pharm.*, 100 (1928), 757.
[3] *Jour. A. Ph. A.*, 17 (1928), 691-698.

they are frequently submitted to classes. The results, so obtained, by some two hundred students who are by no means microchemical experts give a very fair estimation of the value of such a test in the hands of the ordinary worker.

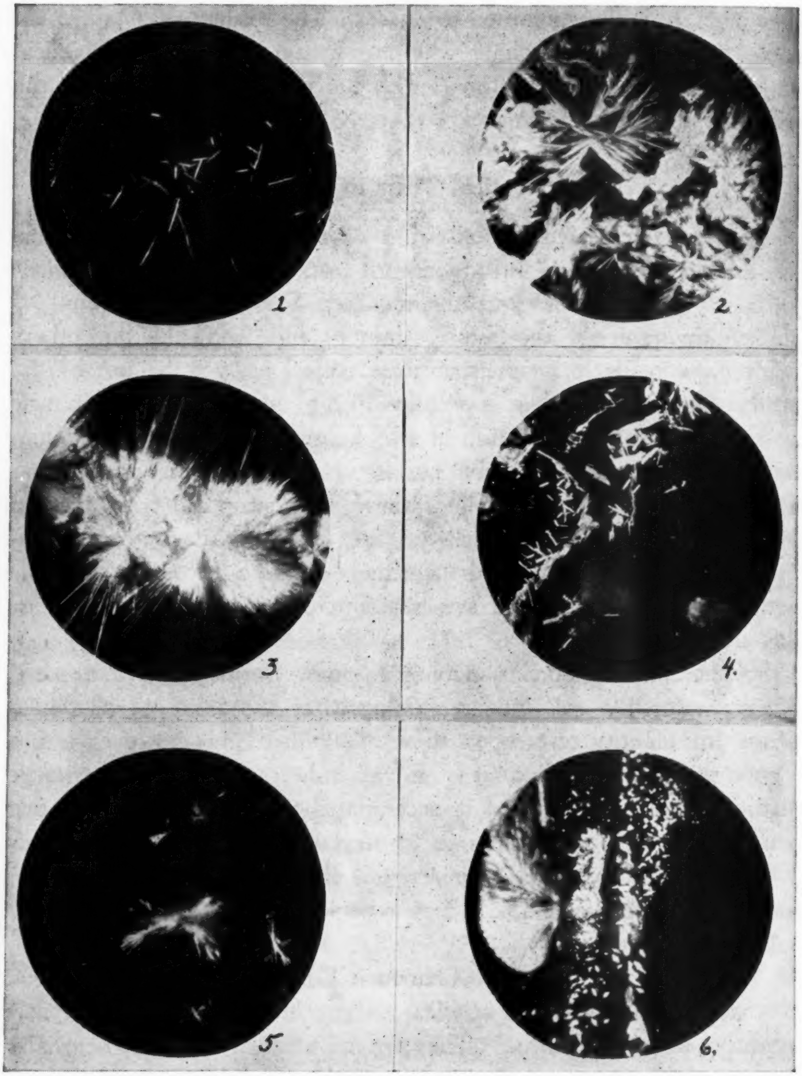
Microchemical Tests in the U. S. P.

During successive editions of the United States Pharmacopœia one notices the gradual introduction of tests into the botanical monographs. Some of these, as the modified Borntrӓger reactions for anthraquinone drugs, the tests for tannins with iron salts, and others might be considered as microchemical reactions, yet the use of the prefix *micro* in these cases is perhaps open to question. The sulphuric acid reaction for strophanthin in strophanthus and the microsublimation of hydroquinone from uva ursi are, however, distinct microchemical reactions. Practically all of these pharmacopœial tests are run by students in the authors' classes, and they are, as a whole, satisfactory and reliable. Should then, more tests be introduced into the botanical monographs, and are phytomicrochemical tests worthy of this introduction?

Other pharmacopœias, notably the new German Pharmacopœia, often employ the solutions remaining after the assay of alkaloidal drugs for identity tests upon these alkaloids. This however is not a good plan, in as much as it is only an indirect test; it involves large quantities of the drug and it necessitates the assay before the test can be run. However, as one of the authors pointed out in this JOURNAL [4] the German Pharmacopœia leads the U. S. P. in direct identity tests on vegetable drugs especially those involving microsublimation.

Through the efforts of Chairman Cook of the Pharmacopœial Revision Committee three articles covering this subject have recently appeared in this JOURNAL.[5] They are the work of Dr. L. Rosenthaler (Tunmann's successor) and carry a plea for the introduction of phytomicrochemical tests into pharmacopœias. Rosenthaler cites many tests, worked out by Tunmann and himself, which are given

[4] *Am. Jour. Pharm.*, 99 (1927), 607-621.
[5] *Am. Jour. Pharm.*, 100 (1928), 93, 455, 757.



EXPLANATION OF FIGURES

Fig. 1—Phenylhydrazone of Cinnamic aldehyde, from Cinnamon.
Figs. 2 and 3—Sodium eugenol from clove.
Fig. 4—Piperine from black pepper.
Fig. 5—Piperine-cadmium compound, from black pepper.
Fig. 6—Opium alkaloids.

Microphotographs were made from drugs by processes described in the text. Figs. 1, 2, 3, 4, 6, 7, 8, 10 and 11 were made with 10x ocular and No. 3 objective. Figs. 5, 9 and 12 were made with 10x ocular and No. 6a objective. Electros have been reduced about one-half from originals.

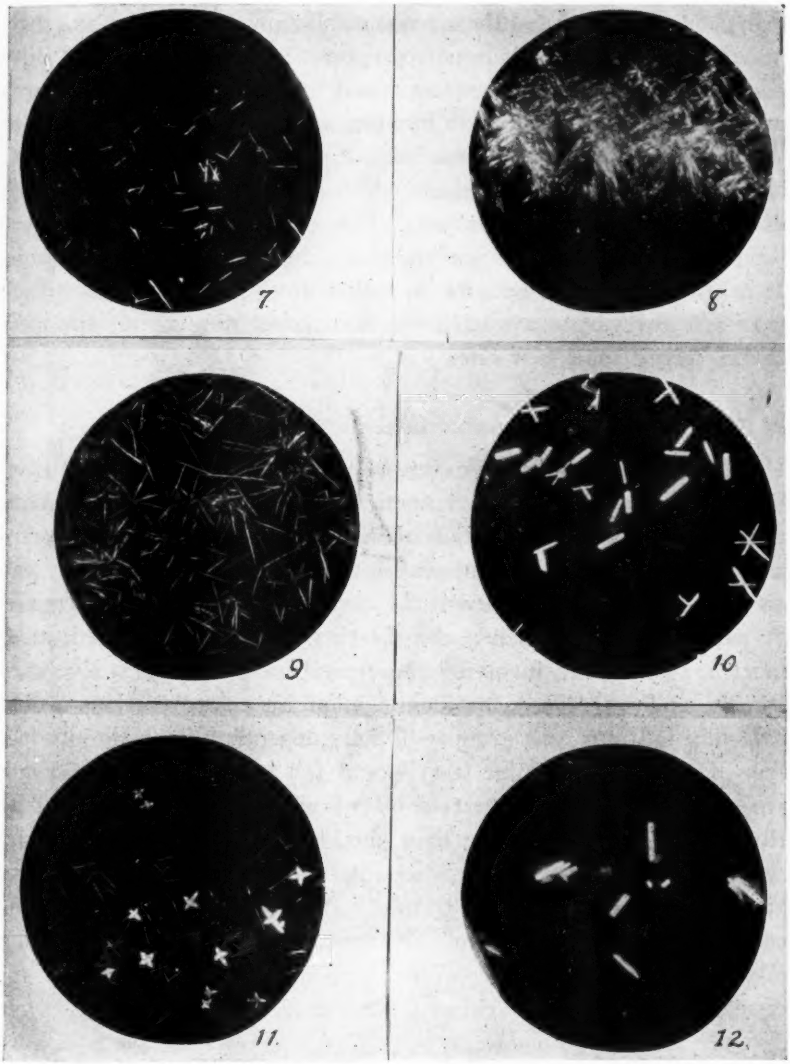


Fig. 7—Cinchona alkaloids.
Fig. 8—Crystals from powdered nutmeg.
Fig. 9—Berberine nitrate from Hydrastis.
Fig. 10—Hydroquinone crystals sublimed from Uva Ursi.
Fig. 11—Anthraquinones sublimed from rhubarb.
Fig. 12—Cantharidin sublimed from Cantharides.

as part of the course in applied phytomicrochemistry at Bern. Chairman Cook suggests [6] that these recommendations be tried out and their practicability and value be reported upon. The authors felt that their position, working with classes equipped to do this type of work was more or less an ideal situation in which to obtain a fair opinion as to the value of these tests. Time has not permitted an investigation of all of them, therefore only those which the authors considered as of exceptional value are discussed. This paper is but a preliminary report and only includes a portion of the work the authors have done. It is furthermore the authors' intention to select certain drugs each year and investigate available reactions concerning them, and perchance devise some new ones.

Phytomicrochemical Tests

Phytomicrochemical tests may be roughly placed into two divisions, (1) those that depend upon the crystallization of the active constituent, or the identification of the active constituent by the preparation of a crystalline compound by organic chemical reaction and (2) those where the identity of the isolated constituent is determined by color reactions. Such a classification is of course limited, in as much as some tests involving the crystallization of the active constituent and its subsequent identification by color reactions would naturally fall into both groups. Others depending upon the production of odors (the coniine test) would fall into neither. Following are given microchemical tests some of which are recommended by Rosenthaler, with which we have obtained particularly pleasing and satisfactory results. These reactions, employed by students, have given positive results almost unanimously. In the case of crystalline compounds we have prepared photomicrographs. These have been taken between crossed nicols (micropolariscope) in order that the crystals appear brilliant against a black field.

Group I. Microcrystallization

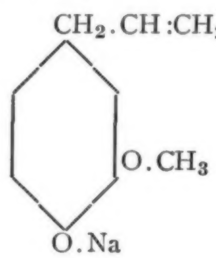
CINNAMOMUM: Extract a few milligrams of the powder with one or two cc. of chloroform in a test tube. A few moments of

[6] *U. S. P. Circular No. 594,* page 2847.

shaking this mixture is sufficient to perform the extraction. Filter one or two drops of this chloroformic extract onto a slide. Allow the chloroform to evaporate spontaneously. To the residue remaining upon the slide add a drop or two of an aqueous 10 per cent. solution of phenylhydrazine hydrochloride and cover with a coverglass. In a very short time little rod shaped crystals of the phenylhydrazone of cinnamic aldehyde appear. (See Fig. 1.) These crystals appear first near the edge of the coverglass but soon may be seen throughout the mount. The formation of phenylhydrazones is a common organic reaction for aldehydes and in this case its microchemical application gives good results. The equation is:

$$C_6H_5.\,CH:CH.CHO + C_6H_5.NH.NH_2 \rightarrow$$
$$C_6H_5.CH:CH.CH:N.NH.C_6H_5 + H_2O.$$

CARYOPHYLLUS: Extract powdered clove as directed under Cinnamon following the process there described in similar manner. After the chloroform has evaporated add to the residue on the slide one drop of a 3 per cent. solution of NaOH saturated with NaBr. Almost immediately needle or spear-like crystals appear (See Figs. 2 and 3), which are often arranged in rosette like bunches and consist of sodium eugenol (sodium eugenolate).



This test would give similar results with Pimenta.

Microextraction on a Slide

In the foregoing tests extraction was carried out in a test tube. An alternative method, and perhaps a simpler one, is direct extraction on the slide. The procedure is as follows: A small quantity of the powder (2 to 5 mg.) is placed on the slide in a little pile about 2 mm.

in diameter. The coverglass is then placed over the powder so that it lies in an oblique position with one end slightly raised. Chloroform (or other solvent) is now introduced at the edge of the coverglass with a pipette or glass rod in such a manner that it will flow under the coverglass and in such a quantity as to completely fill the space between slide and coverglass. The slide is now set aside at room temperature until the solvent evaporates. In the case of chloroform this involves about five minutes. The extracted substances will then be found at or near the edge of the coverglass. In employing very fine powders it is often advantageous to slightly moisten the powder with water before placing it on the slide. This prevents the "flowing out" of particles of the powder into the solvent and becoming annoying in the subsequent examination of the crystalline deposit. The disadvantage of this previous moistening with water however lies in the fact that extraction with the immiscible solvent is slower.

PIPER: A small quantity of powdered black pepper is extracted on the slide with chloroform as described above. After the chloroform has evaporated prismatic crystals of piperine (See Fig. 4) are seen near the edge of the coverglass. These may further be identified by brushing over the area with concentrated hydrochloric acid and adding several very small crystals of cadmium sulphate (or cadmium acetate) to the liquid. The formation of a crystalline deposit consisting of fine needle-like crystals soon takes place. (See Fig. 5.) The fine crystals of this piperine cadmium compound are often arranged in little rosette aggregates. In practically all cases the crystals of piperine were obtained. The subsequent resolving of them into the piperine cadmium compound was however not entirely satisfactory. The difficulty is one of technique.

Ammoniacal Chloroform

An excellent solvent for the microextraction of alkaloids is ammoniacal chloroform. This is prepared by shaking chloroform with ammonia water in a separatory funnel. After separation the lower chloroformic layer which has absorbed ammonia is withdrawn and employed as a solvent. This reagent should be kept in tightly stoppered bottles, it perhaps being better to prepare the reagent as its use is desired.

Opium: Extract opium on a slide with ammoniacal chloroform. After evaporation of the solvent crystals of the opium alkaloids appear at the edge of the coverglass. (Fig. 6.) This crystalline deposit consists chiefly of prisms. Their identity may further be established by treating with formalin-sulphuric acid. With this reagent the crystal zone takes on a violet color. If a drop of arsenic-sulphuric acid is added and heat carefully applied the crystal zone takes on a red color. The opium reactions were not submitted to the classes as opium is not included in the drugs studied in the pharmacognosy laboratory. The results of some twenty determinations in the authors' hands however gave satisfactory results.

Many other tests are available for opium alkaloids such as the potassium-mercuric-bromide reaction [7] and the ferric ammonium sulphate test for meconic acid. While the author's studies relative to these tests have not been completed it might be mentioned that the potassium-mercuric-bromide test for morphine has not, as yet, given satisfactory results in all cases.

Cinchona: Mount the powder in a 2 per cent. solution of NaOH in 50 per cent. alcohol, covering with a coverglass. Heat gently over a micro-burner replacing the evaporated alcohol with water. After cooling the field will be filled with rod-like crystals of the free alkaloids. These occur singly or occasionally crossed into stellate groups (Fig. 7). This reaction gives splendid results in all cases. Rosenthaler mentions that the crystals so formed may be taken up with acetic acid and recrystallized with iodic acid. This latter reaction however, has not been investigated.

Myristica: Extract powdered nutmeg on a slide with chloroform. After evaporation bunches of fine needle-like crystals in "bush" and "feather" form appear at the edge of the coverglass. (Fig. 8.) The composition of these crystals has not been determined. They may consist of myristicin or of myristic acid. Ordinary histological phloroglucin-hydrochloric acid reagent applied to the crystal region gradually turns it red. (Allyl group reaction.) Results with nutmeg were satisfactory in most cases, yet the formation of crystals

[7] *Am. Jour. Phar.*, 100 (1928), 761.

was at times indistinct, due perhaps, that considerably fatty material is also extracted.

HYDRASTIS: The U. S. P. X already carries a microchemical test for hydrastis depending upon the crystallization of berberine sulphate with sulphuric acid. Perhaps a slightly better method for the microcrystallization of berberine salts consists of heating the powder on a slide with water. After cooling a drop of nitric acid is added to the mixture with the result that shortly several needle-like crystals of berberine nitrate are formed, which often occur in bunches (see Fig. 9). This latter method seems better than the present U. S. P. method both in reliability and in quantity of crystals formed.

If hydrastis is extracted on a slide with ammoniacal chloroform the alkaloids crystallize at the edge of the coverglass in little plates. If a drop of vanadic-sulphuric acid (sulphuric acid with 1 per cent. ammonium vanadate) is added and the zone viewed with the microscope it takes on a violet color which however soon fades. (This color is due to hydrastine.) The hydrastis tests described gave good results, the formation of berberine nitrate rather than the sulphate being perhaps the better test. In ammoniacal chloroform extraction the crystals are occasionally indistinct but the crystal region always gave the vanadic acid test.

Microsublimation

Many drugs have sublimable constituents and in several cases these constituents sublime in crystalline form. Subsequent tests may be run upon these sublimates, *e. g.*, if cinnamic aldehyde is sublimed from cinnamon and the afore-described phenyl hydrazine test is run upon the sublimate, crystals of cinnamic aldehyde phenylhydrazone will be formed. With many drugs, however, the constituents do not lend themselves to simple miscrosublimation and with some this process must be carried out in a vacuum. Such cases are, of course, too intricate for pharmacopœial inclusion. There are however many drugs which give good results with ordinary microsublimation. The present U. S. P. includes two such cases, the sublimation of hydroquinone from uva ursi and the sublimation of benzoin. In the later case the behavior of the sublimed cinnamic and benzoic

acids towards polarized light serves to differentiate between the two benzoins. While the U. S. P. directs benzoin to be sublimed in a test tube, microsublimation upon a slide gives much better results, the sublimates being much easier to study with the microscope.

Several methods may be employed for simple microsublimation. The authors prefer the watch glass and slide method. Five to 10 mg. of the powder are placed in a shallow two-inch watch glass. The slide is placed over the powder in such a manner that it rests upon the edges of the watch glass but does not touch the powder. There should be a space of one to two mm. between the powder and the slide. The whole is then placed upon a small asbestos sheet or wire gauze and suspended 8 to 10 cm. directly above a microburner. The flame of the microburner should be not more than one centimeter high. Heat is then carefully applied in this manner until a sublimate forms on the slide. This requires from five to ten minutes depending upon conditions. The sublimate is then examined dry under the microscope, and may be subjected to subsequent microchemical tests. The authors submit three drugs readily lending themselves to microsublimation.

Uva Ursi: Microsublimation of powdered uva ursi by the above process yields prismatic (and occasionally feather-like) crystals which polarize light with a brilliant display of colors. (Fig. 10.) Arbutin, a glucoside present in the drug is decomposed after the following equation into hydroquinone which constitutes the sublimate.

$$\underset{\text{(arbutin)}}{HO.C_6H_4.O.C_6H_{12}O_5} + H_2O \rightarrow C_6H_{12}O_6 + \underset{\text{(hydroquinone)}}{C_6H_4(OH)_2}$$

Rosenthaler [8] states that the hydroquinone may be further identified with p-nitroso-dimethylaniline, a reaction which the authors hope to investigate in the future.

Rheum: Free anthraquinones sublime readily but sublimation in glucosidal combination is usually more difficult. Rhubarb contains a considerable free anthraquinone content and readily gives a sublimate of needles, prisms or feather aggregates depending upon con-

[8] *A. J. P.*, 100 (1928), 461.

ditions of time and temperature. Fig. 11 shows both needles and crossed prisms in the same field. If the sublimate is subsequently treated with sodium or potassium hydroxide the characteristic red anthraquinone reaction may be observed.

CANTHARIS: Cantharidin may be sublimed from powdered cantharides in prismatic rods. (Fig. 12.)

Group II. Color Reactions

Many of the tests now included in the alkaloidal monographs of the Pharmacopœia may be performed upon microextracts of crude drugs. There are however several cases where interfering substances are extracted simultaneously with the alkaloids so that, as a whole this subject needs considerable investigation. A few reactions with which we have had considerable success in class work are submitted herewith.

IPECACUANHA: The powder is treated with ammoniacal chloroform on the slide. After evaporation of the chloroform a drop of molybdic sulphuric acid and a drop of concentrated hydrochloric acid are added. Green zones appear near the powder while in more remote places violet ones appear. Both fade quite readily, the green zones fading more rapidly.

NUX VOMICA: Extract with ammoniacal chloroform on a slide. After evaporation add a drop of vanadic-sulphuric acid at the edge of the coverglass. The zone near the edge assumes a violet color due to strychnine. Add a drop of concentrated nitric acid to a similarly prepared specimen. Little zones of orange red will appear due to brucine.

COLCHICUM: If a drop of concentrated HCl is added at the edge of the coverglass of an ammoniacal chloroformic extract of either colchicum seed or corm the region takes on a yellow color due to colchicine.

HYOSCYAMUS, BELLADONNA, STRAMONIUM: Rosenthaler [9] describes the well-known (Blütenduft) blossom odor test for atropine

[9] *A. J. P.*, 100 (1928), 759.

and hyoscyamine. His method is better than the usual application of this test, yet there is a question as to the value of this test to one who has not become familiar with this characteristic "new-mown-hay" like odor.

Comments

1. Microchemical reactions upon crude drugs involving the bringing of the active constituents into tangible form, so that they may be seen and subsequent test reactions run upon them should form a very important part of pharmacognostical instruction.

2. The inclusion of additional microchemical reactions as identity tests into pharmacopœial monographs is strongly advised.

3. In the selection of phytomicrochemical tests for pharmacopœial identity tests three things are essential:

a. The test must require the minimum of apparatus and technique. In other words it must be simple to perform.
b. The test must be reliable, that is, it must give positive results in every case. The tests discussed in this paper, are, the the authors believe, representative of this type.
c. The tests must serve to identify the drug, that is their reaction must be characteristic for the drug which they represent.

4. The subject of phytomicrochemical reactions requires considerable investigation. It is hoped that other workers will try the reactions discussed herein as well as other similar reactions, so that when the time arrives for the selection of further such tests for pharmacopœial and National Formulary inclusion data relative to their reliability will be available.

5. The authors recommend to the attention of Subcommittee No. 5 of the Revision Committee of the U. S. P. and the corresponding committee of the National Formulary the herein described tests for consideration. It is hoped that some of them together with other available reliable phytomicrochemical tests will receive consideration for inclusion in the monographs as identity tests.

Pharmacognosy Laboratory.
University of Illinois
School of Pharmacy.
June, 1929.

PHARMACOGNOSY NOTES

By L. Rosenthaler

Communications from the Pharmaceutical Institute of the University of Berne*

1. Microchemical Tests for Nitrates in Plants

THERE IS A PLENTIFUL supply in summer of the stems of *Atropa belladonna* and *Datura stramonium* to carry out tests for nitrates in the phytomicrochemical course, but in the autumn the nitrate content is very low, and material kept in alcohol is unreliable. It is desirable to have suitable material available at all seasons. I have examined some powdered drugs for nitrate-content, but this method is also unreliable, as plants that contain nitrates when living may suffer material diminution later. (v. Couperot, C. r. 1909, 149, 957).

For detecting nitrates in plant tissues, the following are used:

1. Diphenylamine sulphate. This produces a deep blue.
2. Nitron (a complex synthetic first applied as a test for nitrates by Busch). One gm. in 10 cc. of 5 per cent. acetic acid gives clusters of needles of nitron nitrate.
3. Alpha-dinaphtho-methylamine (suggested by Rupe). 10 per cent. solution in 50 per cent. acetic acid. It forms with nitrates clusters or rosettes of needles which are the amine nitrate.

These reactions are liable to error. The diphenylamine compound may give blue with other oxidizing substances, most of which, however, are not present in plants. Substances interfering with the reaction may be present. (v. O. Tunmann, Pflanzenmikrochemie, 83). Nitron precipitates several anions, for istance oxalate and thiocyanate anions (v. Visser, *Chem. Centralb.*, 1907, I, 302). It has been stated that nitron precipitates salicylates, but this is due to overlooking the fact that the reagent contains acetic acid which sets salicylic acid free.

Alpha-dinaphtho-methylamine forms a series of difficultly soluble salts. Halides, except fluorides, give crystalline precipitates; fluorides amorphous forms. Oxalate is difficultly soluble. Meconic acid gives a precipitate. Errors can be avoided as if the microchem-

**Pharmazeutische Zeitung,* 1929, No. 5.

ical reaction is checked by the color reactions. The nitron reagent is allowed to act until the characteristic needles are produced. The liquid is evaporated to dryness and the residue treated with diphenylamine sulphate, when characteristic blue spots appear if nitrates were present. I have tested in this way many drug powders. The three reactions occurred with available powders of *Fol. belladonnae, Fol. hyoscyam., Fol. nicotin., Fol. stramon., Rad. belladon,* and *Herb. Card. benedict.*

These can, therefore, be used at any time for demonstrating nitrate tests. Differences were noted with *Herb. Cannab. indic.* and *Laminaria.* With the former the crystals formed with nitron were scanty and with diphenylamine only a few blue points were noted. With Rupe's reagent many crystal rosettes were formed. This seems to be due to the chlorides present, as is stated to be the case in this drug. With *Laminaria* the diphenylamine reaction was negative; with nitron only a few scattered prisms were noted, but with Rupe's reagent rosettes were produced. I think that this result is due to iodine in Laminaria, probably in inorganic association, as can be easily demonstrated with ferric chloride and starch.

2. Two South American Cinchona Barks

Although in a few pharmacopœias, *e. g.,* those of Germany and Switzerland, the Java bark (from *C. succirubra*) is official, some S. American barks are important. In the London and Hamburg markets considerable amounts of these of differing grades are handled. In Hamburg the following are offered: Calisaya (cult.) Equador, Guayaquil, Huanuca, Cartagena, Naradjada monopol, Castrona, Loxa, Maracaibo, Durasnello. As there is nothing available in literature concerning Castrona and Naradjada (given also as Naranjada) it seemed of interest to investigate them. Specimens were kindly furnished by the firm of Caeser and Loritz, to which my thanks are due.

Castrona Bark. Flat forms and half-tubes approximately 50 cm. long 5 broad and 0.65 cm. thick. The outer and inner surfaces, where not covered with cork or outer bark cells, are reddish brown and in spots bright red. In the flat forms the outer surface shows irregular longitudinal furrows, and the inner surface numerous parallel ones. In the half-tube forms, longitudinal furrows are lacking on the outer surface, but coarse cross-hatchings are present. On heating in a test-tube white vapors appear followed by reddish-brown, and

finally a small amount of brown-purple tar. Latex vessels are lacking in the cross section but much sclerotic tissue is noted. The bast fibers are in radial groups, mostly from 790 to 900 mu. long. Starch granules spherical, rarely oval, single or in groups (up to four). The total alkaloid content was 3 per cent. The bark is of the Scrobiculate type.

Naradjada Bark. Flat forms and half-tubes up to 45 cm. long, 4.5 wide and 0.8 thick. Outer surface mostly smooth, except that it is broken in places by shallow or deep depressions. The portions free from outer bark are brownish red; the inner surface is the same. Fracture in the outer layers smooth, in the inner, fibrous. The heat-test gave at white then slightly red vapors and brownish tar. In this bark also, no latex vessels were observed. The outer portion is sclerotised and some stony structure is found also in the inner portion. Besides the normal cinchona bast fibers, the lumen of which is mostly clogged by thickening of the walls, there are numerous unusually long bast fibers. In the radiating direction the bast fibers are discontinuous, but in tangential section well-marked rows are noted. The length of the bast fibers is on the average greater than those of the Castrona bark, the longest showing 1275 *mu*. In many cases, however, the length was from 900 to 1200 *mu*. The Naradjada bark is rich in oxalates, especially in the medullary rays, and poor in starch; the granulas are single or grouped up to five.

The total alkaloid content was 2.6 per cent. The general structure of this bark shows much similarity to the Pubescens type, which according to Berg, is that of the yellow barks.

3. Santonin-free Flores Cinae

I come back to this topic, that I have previously treated (*Pharm. Zentralhalle,* 1926, *67,* 211) on account of an experience in assaying *Flores cinæ pulvis* in our Institute laboratory. Evidence of the presence of santonin in the sample could not be obtained. I ordered more material from the supply-house, expressly stating that the material was to be used for determining the santonin content. Even this did not contain santonin in amount sufficient to be detected by the usual tests. A definite reaction was obtained only when a very old sample was used.

These results show that santonin-free *Cina* is on the market and liable to be dispensed so that it is absolutely essential that dispensers

should test the material. Microscopic examination will, as a rule, not suffice, since samples containing the important principle are essentially the same in structure as those not containing it, the latter being, probably, a biochemical variety. A chemical test must be made but it is not always necessary to carry out the difficult quantitative procedure. A little of the powder is moistened with water extracted with chloroform and the cover glass placed on. After the chloroform has evaporated, the edge of the cover glass is gently heated with sodium methylate. In the presence of santonin the glass will become orange-red. If the test is negative the quantitative analysis will not be required, but if positive, this must be done, as it is possible that an insufficient amount of santonin is present. The sodium methylate reagent, suggested by Gilg and Schurhoff, is preferable to the reagent suggested by me (alcoholic potassium hydroxide). It is prepared by dissolving 10 gm. of sodium in 50 cc. of methanol.

4. Japanese Ginger

Hanausek (*Zeitschr. Allgem. oesterr. Apotheker Vereins,* 1889, *20,* 465) first reported on Japanese ginger. He described it as thin, ribbon like, sometimes peeled, sometimes not, covered with starch powder on the outside, which sometimes also occurs on the inside. The starch according to Hanausek consists of small granules of elliptic shape sometimes single but more often grouped. A. Tschirch (*Handbuch der Pharmakognosie,* 2 Abt. P. 1049) doubts these statements. He doubts the Japanese origin of this ginger and also states that he has never seen starch granules as those described by Hanausek.

It is well known, however, that Japan produces much ginger. According to A. Tunmann (1910) the Japan ginger has replaced the Cochin ginger on the European market, amounting in 1904 to about one-quarter in 1908 to about one-third of the total importation. In Japan there are the grades, Kinki, Tuegoku, and Shilaku. The one year old rhizome is used at the table with salt, and the two-year-old is used as a remedy and as an appetizer.

A small piece of Japanese ginger, which I obtained by courtesy of Professor Bredemann in Hamburg, enabled me to check the figures and statements of Hanausek. My results were in perfect accordance with Hanausek's, particularly as to the character of the starch. Single and grouped starch granules are present, of which the sizes represented by the following figures, all dimensions in *mu,*

of which the numerator is the length and the denominator is the width.

42/28 28/24.5 28/24.5 35/24.5 45.5/30 35/26 35/26 44/28 21/21 21/14 26/17.5 17.5/14 17.5/14 17.5/15 16/14 14/10.5 17.5/10.5 21/17.5 13/10.5.

The grains grouped together are mostly of equal size. On the other hand, the anatomical structure of Japanese ginger is identical with other sorts. Large oil cells with yellow content are present in great number. Neither the vessels nor the fibers gave a red with phlorogulcinol hydrochloric acid. The vessels are frequently associated with tubes of tannin.

5. A Test for So-called Indian Tragacanth

A sample of powder of so-called Indian Tragacanth (also called Sterculia gum or Sterculia Tragacanth) possessed the property to form a gel with 50 per cent. alcohol. As tragacanth powder does not possess this property, the reaction can be used to identify this adulteration. The property of swelling was noted in a mixture of genuine tragacanth and Sterculia Tragacanth, even if this mixture only contained 5 per cent. If 0.5 per cent. of the mixture is shaken with 5 gm. of alcohol for half an hour, the mixture should not show a gel formation, and it should be easy for the tragacanth to be shaken from the bottom of the container.

THE DETERMINATION OF CHLOROFORM IN SYRUPS*

By J. G. Roberts and Allen F. Murray

SEVERAL METHODS have been suggested at various times for the estimation of chloroform in syrups. These methods in the main have consisted in the distillation of the chloroform from the syrup and the saponification with an alkali hydroxide. The alkali chloride being estimated either volumetrically or gravimetrically. Of the several methods recommended none seem to take into sufficient consideration the extreme volatility of chloroform. This property of chloroform and its slight solubility in some syrups are the foremost

*Presented to the Pennsylvania Pharmaceutical Convention at Bedford, Penna., June, 1929.

reasons why results are not always concordant. Of the methods examined the one submitted to this laboratory by L. E. Warren† gave the most concordant results when precautions were taken to eliminate the foregoing sources of error.

REAGENTS:

Alcoholic Potassium Hydroxide.—Thirty grams of potassium hydroxide reagent (quality free from chloride) dissolved in 30 c.c. of water with sufficient methyl alcohol (reagent quality) to make 100 c.c. Allow to stand three days, then pipette from the top with a clean pipette (do not attempt to filter).

Alcohol.—U. S. P. (95% ethyl alcohol).

Nitric Acid.—U. S. P. (68% nitric acid).

Silver Nitrate.—Ten grams U. S. P. silver nitrate dissolved in sufficient water to make 500 c.c.

Phenolphthalein.—.1 gram phenolphthalein dissolved in sufficient 95% alcohol to make 100 c.c.

DETERMINATION:

Place 1 gm. of calcium carbonate and 75 c.c. of alcohol in a 250 c.c. Kjeldahl distilling flask and carefully pipette into this mixture 20 c.c. of the syrup to be examined, being careful not to agitate the mixture and to keep the tip of the pipette just below the surface of the liquid. Connect with a straight bore condenser and distill into a previously cooled citrate bottle immersed in cracked ice and containing 25 c.c. of alcoholic potassium hydroxide solution into which the tip of the delivery tube extends.

When 70 c.c. of the alcohol has been distilled over (this can be judged by previously marking the bottle) discontinue the distillation and wash the receiving tube with about 10 or 15 c.c. of distilled water collecting the washings in the citrate bottle. Stopper the bottle and gently agitate, taking care to prevent the solution from coming in contact with the rubber washer.

Allow to stand over night at room temperature, then heat on a steam bath for one hour. Remove from the bath and allow to cool, then empty the contents of the bottle into a 500 c.c. beaker and wash the bottle with distilled water until the washings are no longer alkaline to phenolphthalein, adding each washing to the main solution. Now

†Drug Research Unit; Food, Drug and Insecticide Administration, United States Department of Agriculture.

add 15 c.c. of nitric acid and an excess of silver nitrate, stir well and allow to stand in a dark place for fifteen minutes.

Collect the precipitate upon a Gooch crucible which has been previously prepared, dried at 105° C. and weighed. Wash the precipitate with several portions of distilled water then with 5 c.c. of alcohol followed by a 5 c.c. portion of ether. Dry at 105° C. and weigh.

Each gram of silver chloride corresponds to 0.27765 gram of chloroform. Assuming that 1 minim of water weighs 0.06161 gram and that the specific gravity of chloroform is 1.475 (average of the U. S. P. limits), then 1 minim of chloroform weighs 0.090936 gram and basing calculations on 1 fluid ounce measuring 29.57 c.c., the factor for grams of silver chloride to minims of chloroform per fluid ounce is 4.5142 for the 20 c.c. sample.

Summary of Analyses:

Over one hundred and twenty assays were performed in duplicate using 20 c.c. of the sample. These samples ranged in chloroform content from .34 minim to 4.64 minims per fluid ounce. Of these duplicate tests 79% checked within .002 gram of silver chloride. The other 21% checked within .005 gram silver chloride. A sample of syrup containing a known amount of U. S. P. chloroform gave 98.7% of the amount taken.

Comments:

The insolubility and volatility of chloroform are perhaps the foremost reasons why most methods give results which are not concordant. To insure more accurate results it has been found necessary before withdrawing the proper amount of syrup for analysis to thoroughly shake the sample. This thorough shaking is imperative because of the separation of chloroform in samples of low alcoholic content. The remaining portion of the sample is then immediately preserved in small completely filled bottles as reserve samples. This is advisable because, when a portion of the sample has been withdrawn, the chloroform is partially volatilized into the remaining space, so that when check determinations are made on the sample the results will be much lower than the first determination. This is particularly noticeable in samples having a low chloroform content.

In pipetting the sample, the adhering syrup is not to be expelled from the tip of the pipette by blowing with the mouth. It is advisable to wash the remaining syrup from the pipette with a few small streams

of water from a wash bottle. This hastens the completion of the operation and minimizes the loss of chloroform.

The distillation may be carried on rapidly. However, it is advisable not to distill the alcohol entirely off, as some syrups contain substances which are volatile in a current of stream and have a reducing action on the silver chloride. When the freshly precipitated silver chloride is allowed to stand for fifteen minutes it becomes more dense, thus facilitating filtration.

It is imperative to heat the solution on a steam bath after standing over night to insure saponification of the last traces of chloroform. If the solution is heated on the bath without standing over night, low results are obtained. The highest and most concordant results were obtained when both precautions were observed.

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—From the Analytical Laboratory of the Smith, Kline & French Laboratories.

THE PLACE OF PHARMACY IN THE BIGGER AND BETTER AGE

By C. Jelleff Carr*

(Abstracted)

THE PAST DECADE has witnessed a great transition with respect to pharmacy, a transition that some are prone to look upon as degrading. It is apparent, however, that changes have occurred behind the store window of alarm clocks that will manifest themselves in the future as having had a definite trend toward a bigger and better phar-

*Mr. Charles Jelleff Carr, the 1929 winner of the National Garvan Chemistry Prize, was born in Maryland, March 27, 1910. He received his early education in Baltimore and at Hanover, Pennsylvania, and completed his high school work at the Evening High School of the Baltimore City College, graduating this year. The Garvan Chemistry Prize consists of a four-year scholarship to any recognized university in the United States with $2000 cash for maintenance during the four collegiate years. Although still a youth of 19, Mr. Carr has exhibited a number of interesting characteristics which are destined to carry him far into his chosen field of endeavor, namely, pharmaceutical chemistry.

macy. The adoption of scientific methods by the pharmacist and pharmaceutical manufacturer actually represents an acceptance of a greater responsibility and a greater field of service than ever before in the history of the profession.

That grand old master of chemistry, Prof. R. W. von Bunsen, once said, "There are two classes of men: first, those who work at enlarging the boundaries of knowledge, and secondly, those who apply that knowledge to useful ends." It is into this second class that those

C. Jelleff Carr

who follow the profession of pharmacy fall. Theirs is the utilitarian side of that great white science called chemistry. Much has been written concerning this first class of men. Only little, however, has been written concerning the second class, notwithstanding the fact that it is to the second class that mankind is indebted for his direct benefit.

We today dare not question the value of scientific investigation carried on with the single motive of discovering new truths, yet in

some respects this sort of discovery is of a meager sort if no practical application is made of the knowledge gained thereby.

To foresee the possibilities of a discovery and to transform them into shape for some practical purpose is a trait not commonly possessed by scientific investigators. Yet in the service of silencing suffering it falls to the lot of the pharmacist to do exactly this. This indeed is the difficult task of standing with one foot in that realm of sovereignty, the land of the search for truth, while the other rests in the practical life of his fellow beings. And in these dual capacities he has always the need of realizing that he should not become the galley slave of short-sighted commerce. To do so would mean the breaking down of all that the centuries of the past have contributed to the building up of this outstanding line of endeavor.

A splendid example of the modern place of pharmacy is unfolded before one as he walks along the corridor of a modern pharmaceutical research laboratory. Here indeed are the altars of truth, here are workers toiling upon the frontier of knowledge. Some are like Liebig, that monumental personage of pharmacy, who represented a romantic school—those who restlessly rush from one problem to another; others like Wöhler, a true representative of the classic school, who quietly but thoroughly investigate each subject—here is the heart of pharmacy, here the true heroes of the pestle and mortar. These men are making pharmacy bigger and better, they are accentuating the tempo, putting it in gear with the trend of the nation, for without this help it will fall into discard, to be relegated to the museum and gazed upon by holiday crowds beside the other objects of antiquity.

In this age the quality of drugs that line the druggist's prescription counter is directly proportional to the happiness and health of the nation. Each queer compound represents the dream of some scientific investigator to obtain a specific relief for some particular disease. Many are miserable failures, some represent fair success, while but few represent perfection, as exemplified by quinine and salvarsan. Even as this is written others may be at hand. Truly to the thinking individual the compounding of these drugs represents a classical art and the compounder an artist whose name should be a benediction.

Those who bemoan existing conditions and insist that the corner drug store is fast becoming a quick lunch counter should consider the recent announcement of the Department of Commerce at the American Drug Manufacturers Association. In the one city named, Balti-

more, the department announced, the sales of drugs, chemicals, and prescriptions represented 75 per cent. of total sales, while toilet articles carried only 9 per cent, other commodities collectively had lower percentages of sales down to rubber goods with a 1 per cent. sale. Surely this seems positive evidence that after all drug stores are still *drug* stores.

We moderns have come to look upon the drug store as representing the entire profession of pharmacy. According to Prof. Ivor Griffith this viewpoint is wrong. He says:

> "The tremendous drug industry—huge collecting drug organizations and milling concerns, large organic and inorganic chemical manufacturers, immense pharmaceutical establishments, biologic laboratories, control laboratories, institutes of pharmaceutic research—all of these are the pharmacies of today, with the corner drug store only a very small corner of a very large picture."

Undoubtedly here we have a bird's eye view of the modern drug industry. Truly this represents the bigger Pharmacy—bigger than in the day of our forefathers, and destined to grow even greater. Bigger, yes—and better, too!

What is more heartrending than the passing of an old friend—a friend you knew well, upon whom you could always rely in every contingency? Shall it come to pass that the men of pharmacy today will see the passing of their old friend Pharmacy, as they knew it when they were boys? Perhaps they shall; surely indications seem to point in that direction. If within the next few years that pharmacy as Liebig, Scheele, Remington and Caspari knew it passes from the drug store, it will not die. No, it will be immediately taken into the cradle of science where it is even now fast finding a corner, there to be fostered and enriched until on a new day it shall blossom forth a new, a bigger, a better pharmacy for all its hardships.

ABSTRACTED AND REPRINTED ARTICLES

THE DETERMINATION OF SMALL AMOUNTS OF ALCOHOL IN THE HUMAN SUBJECT*

By John Evans, F. I. C., and A. O. Jones, M. A., F. I. C.

WHEN A PERSON drinks alcohol some of it is absorbed as such into the blood, and as this blood passes through the kidneys a certain amount is excreted in the urine.

As early as 1915 Widmark published results of the examination of the urine of persons arrested for drunkenness, and since then the subject has been investigated by others. The object of this paper is to draw attention to an extensive series of investigations made at Sheffield University by Professor Mellanby and Dr. Southgate in 1924-1925, in order to obtain information as to the rate of absorption of alcohol into the blood and the rate of its excretion in the urine, and more particularly to draw attention to the ingenious apparatus employed by Dr. Southgate to determine small amounts of alcohol in blood and urine. The apparatus is so designed that only 2 c.c. of the sample are required for a single determination.

We have had considerable experience in the use of the apparatus, and find it easy to manipulate, and, judging by the agreement obtained between duplicate determinations, highly accurate. As it may be necessary at any time in forensic practice, or even in the Public Analyst's ordinary work, to determine alcohol in low concentrations, we think that this method ought to be more widely known.

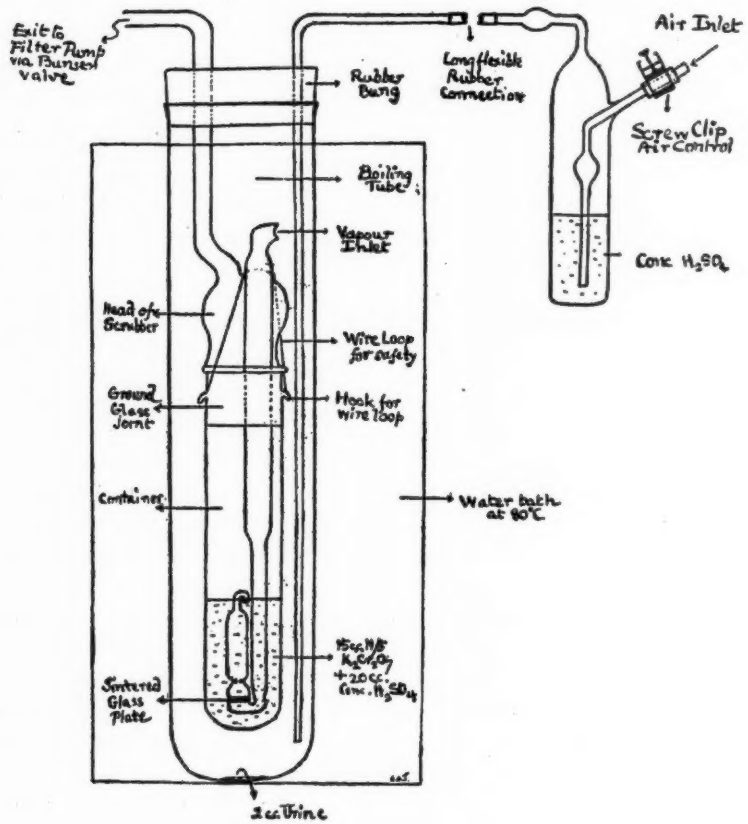
SUMMARY OF THE PROCESS.—Two c.c. of urine are evaporated slowly at 80° C. in a current of air which has previously been washed by passing it through concentrated sulphuric acid.

The mixture of air and alcohol vapour is led through a mixture of 15 c.c. of $N/5$ potassium dichromate solution and 20 c.c. of concentrated sulphuric acid in an apparatus specially designed to promote efficient interaction. The alcohol is oxidised to acetic acid at the expense of some of the dichromate, in accordance with the equation—
$CH_3.CH_2OH + 2O = CH_3.COOH + H_2O$.

*Reprinted from *The Analyst* (Great Britain).

The unreduced dichromate is determined by causing it to liberate iodine from potassium iodide and titrating the liberated iodine with $N/10$ sodium thiosulphate solution. The reduced dichromate is thus known by difference, and is calculated to its equivalent of alcohol.

Description of the Apparatus.—The apparatus is a modification, devised by Dr. Southgate, of an apparatus used by Canan and



Sulzer, and consists of three parts: a boiling tube, a container, and a scrubber.

The large outer boiling tube is closed by a rubber bung pierced by two holes. Through one hole passes a narrow glass tube reaching nearly to the bottom of the boiling tube. The inlet of this tube is connected with the sulphuric acid air-washer. Through the other hole

passes the exit tube of the scrubber, which is connected with an ordinary filter pump.

Inside the boiling tube is the container, in which the acid dichromate solution is placed. By means of a ground-glass joint this container is fitted to a glass bulb-shaped head, which is in communication with the exit tube to the pump.

Fused into this glass head is a wide tube, the inlet of which is open to the interior of the boiling tube. At the other end of this tube, which reaches nearly to the bottom of the container, is an ingenious scrubber, containing a sintered glass plate. The scrubber is immersed in the acid diochromate solution, and 2 c.c. of the urine to be examined are placed in the outer boiling tube. Fifteen c.c. of the $N/5$ diochromate solution are placed in the container, and 20 c.c. of concentrated sulphuric acid added, the container being kept cool in water. The container is then fitted to the scrubber head, wired on for safety, and by means of the rubber bung the boiling tube is attached. The narrow inlet tube is connected with the sulphuric acid air-washer, and the exit tube with the pump. When a steady aspiration is established the apparatus is weighted with a heavy weight and almost completely immersed in a water-bath maintained at 80° C. The current of air draws the volatile products of evaporation of the urine through the dichromate solution, the sintered glass plate of the scrubber reducing the vapour to a stream of minute bubbles and thereby ensuring rapid and complete oxidation. When evaporation is complete (in 20-30 minutes) the apparatus is removed from the bath, the boiling tube disconnected, and the dichromate solution transferred to a litre flask.

The container and scrubber are washed several times with water by suction at the pump, and the combined liquids are diluted to about 500 c.c. About 1 grm. of solid potassium iodide is now added to the solution, and the liberated iodine is titrated with $N/10$ sodium thiosulphate solution, starch being used as an indicator. Factor: 1 c.c. of $N/10$ thiosulphate $=$ 0.00115 grm. of alcohol.

Manipulation of the apparatus is easy, and with ordinary care accurate results are obtained. The following details and precautions readily suggest themselves to the operator.

A steady uni-directional flow of air is essential, and its rate of flow can be controlled by means of a screw-clip on a piece of pressure-tubing on the inlet to the air-washer. The mercury column of the pump should stand at 4-6 inches, and the evaporation of the 2 c.c. of urine should be complete in 20 to 30 minutes.

An obvious danger is a sudden reduction in the aspiration, which may cause alcohol vapour to be blown back into the air-washer and retained there. It is therefore advisable to interpose a Bunsen valve between the exit from the apparatus and the pump. A reversal of the air-current, due to failure of the pump, is thus avoided.

For the same reason a vigorous and steady aspiration should be established before the apparatus is placed in the water-bath; otherwise expansion of the air in the boiling-tube may drive alcohol vapour into the air-washer.

Full dilution of the dichromate solution is, of course, essential, and care must be taken that no undiluted liquid remains on the sides of the litre flask, as it is sufficiently acid to liberate iodine independently of the dichromate.

The urine should be tested for freedom from glucose, as the presence of a fermentable carbohydrate makes the interpretation of the results impossible, as some of the alcohol might be derived from the sugar.

It is our practice also to test for albumin.

Physiological Relations.—The following information is extracted from a paper by Drs. H. W. Southgate and G. Carter, in the *British Medical Journal* (March 13, 1926, pp. 463-469):—"The alcohol in the blood is related to the amount of alcohol consumed when this is imbibed under constant conditions, and the ratio between the alcohol in the blood and the alcohol in the urine is surprisingly constant and is of the order of 1.35.

The presence of alcohol in the blood is recognisable, even twelve hours after the time of drinking.

The concentration of alcohol in the blood attains a maximum value about one and one-half hours after consumption, and falls at the rate of about 12 mgrms. per hour per 100 grms. of blood.

If the same person consumes equal amounts of alcohol in widely different concentrations, it is found that the alcoholic concentration rises more rapidly, and to a higher point, in the case of the stronger solution. Also, the slower the rate of drinking, the lower will be the maximum concentration attained.

All foods tend to depress the absorption of alcohol from the stomach and intestines and thereby lower the alcoholic concentration of the blood, but some have such a potent action in depressing blood alcohol as to be almost specific. Among these foods bread and milk stand

out pre-eminent. Food however makes little difference to the ratio between blood alcohol and urine alcohol.

It has been shown by Schwersheimer that if abstainers, moderate drinkers and heavy drinkers take the same quantity of alcohol when other conditions are equal, then the concentration of alcohol in the blood is highest in the case of the abstainer and lowest in the heavy drinkers. In other words, a kind of tolerance has been established in the case of the heavy drinker.

FACTORS.—If a sample of urine has been excreted when its alcohol content is at its maximum point (*i. e.*. one and one-half hours after consumption), the following relations can be used to determine the amount of alcoholic liquor consumed:

Whisky.—Ninety-six c.c. of absolute alcohol (= 235 c.c. of whisky) correspond to 200 mgrms. of alcohol per 100 c.c. of urine.

Beer.—Ninety-six c.c. of absolute alcohol (= 1920 c.c. of beer) correspond to 178 mgrms. of alcohol per 100 c.c. of urine.

i. e. for whisky:

Mgrms. of alcohol per 100 c.c. $\times$ 0.04137 = fluid ounces consumed.

for beer:

Mgrms. of alcohol per 100 c.c. $\times$ 0.0190 = pints consumed.

EXPERIMENTAL WORK.—In order to satisfy ourselves as to the working of the analytical process described, and to assure ourselves of the possibilities of the method as a chemical determination of the amount of alcoholic liquor consumed, we made the following experiments.

(1) *With a solution of pure alcohol.* A sample of *Spiritus Vini Rectificatus,* B.P., was taken, and its alcoholic content determined by specific gravity. An accurate 1 per cent. v/v solution was then made, and the alcohol in it determined by Dr. Southgate's method. The amount of alcohol found per 100 c.c. was 0.68 grm.

By calculation from the specific gravity 0.69 grm. of alcohol was present in 100 c.c.

(2) Two samples of urine were supplied by a person who stated that he had taken a quantity of beer at about 7 P. M.

The first sample of urine, excreted at 7.20 P. M., showed 27.3 mgrms. per 100 c.c.

The second sample of urine, excreted at 8.30 P. M., showed 55.5 mgrms. per 100 c.c.

Taking the figure found with the second sample, the consumption of beer works out to 1.05 pint. After the analysis the consumer stated that the quantity taken was one pint.

(3) Sixty c.c. (2.1 fl. ozs.) of whisky, diluted with 60 c.c. of water, were drunk rapidly on an empty stomach. The alcohol in the urine was then determined.

(i) 50 minutes after consumption, 23 mgrms. per 100 c.c.
(ii) 1⅓ hours after consumption, 57 mgrms. per 100 c.c.
(iii) 2¾ hours after consumption, 17.5 mgrms. per 100 c.c.

The maximum figure obtained (57 mgrms. per 100 c.c.) corresponds to 2.3 fl. ozs. of whisky. The quantity drunk was 2.1 fl. ozs.

(4) Two samples of urine were provided by a person who had taken two pints of beer, followed by two small whiskies.

The first sample, excreted 45 minutes after consumption, showed 92.5 mgrms. per 100 c.c.

The second sample, 1¼ hours after consumption, showed 129 mgrms. per 100 c.c.

By calculation from the amount consumed, the maximum concentration of alcohol attained should be 150 mgrms. per 100 c.c.

The necessity for determining alcohol in the human subject, either during life or post-mortem, is one which can easily arise in forensic chemistry. The method described is admirably suited for this purpose, provided that no other volatile oxidisable matter is present.

In the present congested state of traffic in our cities the intoxicated motorist is a danger both to himself and to the public. How little alcohol is required to upset the higher mental faculties (which by a well-known physiological law are affected first) we are not in a position to state—the question is pre-eminently one for the physiologist, but our own experiments show that when a quantity of alcoholic liquor, insufficient to produce intoxication in the ordinary sense of the term, is consumed, the alcohol excreted in the urine can be determined.

We have had the opportunity of determining the alcoholic content in numerous samples of urine taken from persons arrested for being drunk in charge of motor cars.

For comparison, therefore, we append a few of these results to indicate the degree of concentration of alcohol in the urine in cases where large amounts of alcoholic liquors have been consumed.

	1st Sample		2d Sample		3d Sample	
	Time	Alcohol per 100 cc. Mgrms.	Time	Alcohol per 100 cc. Mgrms.	Time	Alcohol per 100 cc. Mgrms.
1.	9.15 p.m.	269	10.00 p.m.	261	11.15 p.m.	202
2.	1.00 a.m.	292	2.00 a.m.	264	—	—
3.	11.45 p.m.	336	1.10 a.m.	302	—	—
4.	8.50 p.m.	395	10.15 p.m.	373	—	—
5.	12.50 a.m.	412	—	—	—	—
6.	5.10 p.m.	268	5.55 p.m.	285	7.30 p.m.	211
7.	1.08 a.m.	342	2.48 a.m.	287	—	—
8.	4.40 p.m.	349	5.05 p.m.	355	—	—
9.	11.15 p.m.	286	12.20 a.m.	243	—	—
10.	4.15 p.m.	293	—	208	—	—
11.	9.00 p.m.	378	9.45 p.m.	338	—	—

In conclusion, we may quote a statement from a paper read by Dr. Godfrey Carter before the Society for the Study of Inebriety: "Two hundred mgrms. of alcohol per 100 c.c. of urine suggests moderate intoxication, 360 mgrms. per 100 c.c. of urine suggests definite drunkenness.

The apparatus (excluding the sulphuric acid air-washer) is supplied by: Messrs. The Scientific Glass Blowing Co., 12-14, Wright Street, Oxford Road, Manchester.

REFERENCES

Southgate, H. W.: *Biochem. J.*, 19, 737.
Canan and Sulzer: *Heart*, 1924.
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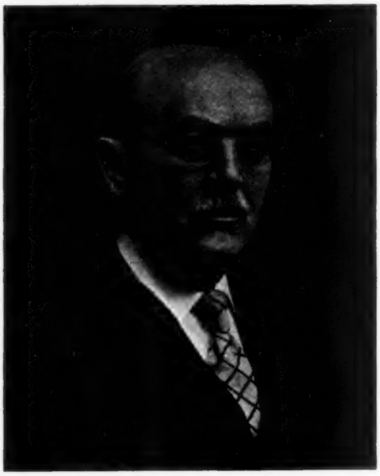
OBITUARY

FREDERICK W. HAUSSMANN

FREDERICK WILLIAM HAUSSMANN, son of William A. and Marie M. Haussmann, one of the foremost figures in Philadelphia Pharmacy, was born in Stuttgart, Germany, on December 9, 1868, and died suddenly of paralysis on July 23, 1929, at Urach, Wuerttemberg, Germany, while traveling with his wife and daughter. He had been, apparently, enjoying good health. He is survived by his wife, Marie, and two daughters, Elsie M. and Mrs. Marie L. Weigand.



Frederick W. Haussmann

He received his school education in Germany, and came to this country at an early age with his parents and three brothers, who survive him.

Mr. Haussmann entered the profession of pharmacy as an apprentice in the store of the late Charles Diik, when thirteen years of age. A few years later he came to know Christian Weiss—also a pharmacist—and this was the beginning of a lifelong friendship that terminated only with the death of the latter in 1918.

He became a student of the Philadelphia College of Pharmacy and graduated with the class of 1890, the subject of his thesis being

"Orange and Turpentine Groups." He early evinced a keen interest in professional pharmacy, and made a number of original investigations, the results of which were published in the AMERICAN JOURNAL OF PHARMACY. His alma mater conferred upon him this year the honorary degree of Master of Pharmacy.

Mr. Haussmann served the community in the vicinity of Sixth and Girard Avenue, as a pharmacist, for forty-five years, and his store was a really ethical store and one of the best equipped in Philadelphia.

In many fields of endeavor he gave unstintingly of his time, his money and himself to the service of the enterprises with which he was connected. He was very active in German-American affairs, being president of the United Singers of Philadelphia and secretary of the Northeastern Saengerbund.

He was a member of the Board of Trustees of the Philadelphia College of Pharmacy and Science, of the Pennsylvania Pharmaceutical Association, and of the American Pharmaceutical Association.

Frederick W. Haussmann loved his profession, and his exemplification of its highest ideals in his daily practice and his splendid personal character brought honor to his profession and lustre to his name. The memory of his work will stay with us long to stimulate and inspire.

MEDICAL AND PHARMACEUTICAL NOTES

THE BIOLOGICAL ASSAY OF ERGOT PREPARATIONS—It was shown some time ago that of the then known constituents of ergot only ergotoxin would produce the characteristic cyanosis and gangrene of the cock's comb. Since the recent isolation of a second alkaloid, ergotamine, it has been shown that this substance also will produce the characteristic discoloration and in sufficient doses gangrene of the rooster's wattles. The U. S. P. method then is an index of the concentration of the two alkaloids, ergotoxin and ergotamine, peculiar to ergot.

The use of the U. S. P. method of assay of ergot, and the epinephrine-reversal method introduced by Broom and Clark yield results practically identical. Both methods determine the alkaloidal content. By both methods the U. S. P. standard fluid extract is approximately the equivalent of a 0.05 per cent. solution of the specific alkaloids,

which is about one-half the value of the standard set up by the research laboratory of the British Pharmaceutical ssociation as suitable for fluid extracts. The British standard is felt to be too high, since examination of the literature seems to indicate that very few specimens of ergot will yield a fluid extract measuring up to its value. It is the authors' opinion that a standard the equivalent of a 0.05 per cent. solution of alkaloids would be more practical. Of the two alkaloids, ergotoxin and ergotamine, the former is found to be slightly but distinctly stronger than ergotamine.

The epinephrine-reversal method mentioned above is based on the ability of these same alkaloids to paralyze or to reverse the response of various tissues to epinephrine. There are several methods. The one most extensively used is that of Broom and Clark, in which the strength of an ergot preparation is determined by its ability to decrease the response of the isolated uterus of the rabbit to constant doses of epinephrine.

Although this method has been examined by a number of investigators, except for a short series in the original paper of Broom and Clark, no comparison of the results of assays by the two methods seems to have been made. The authors' work embodied in this paper supplies that lack. They make a number of observations which seem worthy of record. Some modifications of the methods were found necessary, which they give in detail. The value of the Standard Fluid Extract of Ergot of the U. S. P. has been evaluated in terms of ergotamine, and ergotamine and ergotoxin have been compared with each other.—*By George L. Pattee and Erwin E. Nelson, The Journal of Pharmacology and Experimental Therapeutics, May, 1929, page 85.*

J. K. T.

Standardization of Digitalis Tincture.—F. Wokes (through *Chemist and Druggist,* "Quarterly Journal of Pharmacy and Pharmacology," II, i, 48) summarises, with graphs and tables, the results of examining eighty commercial samples of tincture of digitalis. The British Pharmacopœia requirements assume that digitalis leaves always contain approximately the same amount of activity. But when eight samples of English digitalis leaves were assayed by the cat method they showed an average activity similar to that possessed by the international standard, but a variation in activity between different samples of nearly 140 per cent. Among eighty commercial samples of

the tincture a variation in activity of nearly 400 per cent. was found, twenty-five of the samples differing by more than 25 per cent. from the activity possessed by a tincture prepared from the international standard powder. Samples of tincture of digitalis were biologically assayed both by the cat and the frog method. The average experimental errors were 8.7 and 5.9 respectively. The results by the two methods differed from each other by more than the experimental error in seven cases. On the whole, the frog method gave lower results than the cat method. When the age of these tinctures was taken into account the cat and frog results became consistent. It was found that the frog potency diminishes rapidly and steadily during the first few months of storage until it reaches a level of from one-half to two-thirds of its original value, at which point it becomes fairly constant for some years. The cat potency, on the other hand, decreases much more slowly. Tinctures not more than a month old will give the same results when assayed either by the cat or by the frog method. In the case of older tinctures the results will be different, and further clinical evidence is required to show which is the more accurate estimate of the therapeutic value. If the frog method is to be employed comparison must in every case be made with a standard tincture which has not been made longer than a month.

Federal Court Rules on Drug Labels—A far-reaching decision on the labeling of medicinal preparations has been handed down by the U. S. Court of Appeals for the Ninth Circuit, say the officials of the Food, Drug and Insecticide Administration of the United States Department of Agriculture.

According to the decision of the Court of Appeals, the use on labels of medicinal preparations of language which, when read literally, is not a statement of curative or therapeutic properties, but, owing to attendant circumstances, may be understood as such, brings these labels within the scope of the Federal Food and Drugs Act just as definitely as if direct statements appeared.

This decision was made upon appeal by the United States Government from a judgment entered in the District Court for the Western District of Washington, dismissing a case brought against certain medicinal preparations which, the Government alleged, bore false and fraudulent therapeutic claims on the labels. The Federal Food and Drugs Act, under which this action was brought, is designed, among other things, to prevent the sale in interstate commerce of medicinal

preparations bearing false and fraudulent statements concerning their efficacy in treating disease.

The lower court dismissed the libel on the ground that it failed to allege facts sufficient to show a violation of the law, in that the statements on the labels to which the Government took exception were not therapeutic or curative claims but were merely reports indicating that physicians had obtained favorable results from the use of the nostrum, each "report" being preceded by the statement, "We have received many letters from physicians reporting."

The Circuit Court of Appeals, however, held that language such as that used would tend to engender a belief on the part of possible buyers that the use of the drugs would afford relief. "Unless we discredit their mental competency, such, we must presume, was the intent and expectation of the proprietors," said the Circuit Court. "Their contention is that they have such letters or reports and that that fact constitutes a competent defense, whatever may be the character of the drugs. But if, as is alleged, the drugs are worthless, the proprietors cannot escape responsibility by hiding behind the phrase, 'The doctors say.' Couched in such language, undoubtedly the printed matter makes a more persuasive appeal to the credulity of sufferers from these diseases than if the representations thus implied were made directly upon the authority alone of the proprietors, and for that reason they are not less but more obnoxious to the law."

Furthermore, the court held that the following principle of construction set forth in an opinion of the Supreme Court rendered in a case against vinegar brought under the food and drugs act is conclusive in this case also:

> "The statute is plain and direct. Its comprehensive terms condemn every statement, design and device which may mislead or deceive. Deception may result from the use of statements not technically false or which may be literally true. The aim of the statute is to prevent that resulting from indirection and ambiguity, as well as from statements which are false. It is not difficult to choose statements, designs and devices which will not deceive. Those which are ambiguous and liable to mislead should be read favorably to the accomplishment of the purposes of the act."

Cyanide Poisoning From Polish on Hotel Silver—The shiny, freshly polished spoon or fork may not be the best one to pick out in a cafeteria or hotel dining room, it now appears. A number of cases of acute cyanide poisoning have been traced to polish used on

table silver and other metal kitchen or eating utensils in various hotels in the State of New York, the State Department of Health has just reported. No deaths have been reported so far, but a number of persons have been made seriously ill.

When several cases of illness, apparently food poisoning, were reported occurring in persons who had dined at an upstate hotel, health officers began investigations, following every clue that might lead to discovery of the guilty substance that had caused the illness, whether food or germ. They found that the hotel's silver had just been polished. Chemical analysis of the silver polish used showed that about one-fifth of it was composed of poisonous sodium cyanide. Further investigations disclosed that other hotels and restaurants in the State and in New York City were using this or other cyanide-containing polish for their silver. This fact probably accounts for numerous unexplained cases of severe illness following meals in hotels and restaurants.

One woman, whose work entails considerable traveling, reported having suffered twelve different attacks during a year while stopping at hotels in various cities. Some hotels have already reported that attacks of similar illness among their guests have ceased to occur since this type of silver polish has been discarded.

The Health Department is continuing studies to determine the extent of the use of cyanide compounds in the polishing of cooking and eating utensils in public eating places throughout the State.—(*Science Service.*)

NEWS ITEMS AND PERSONAL NOTES

A Centenary in the Essential Oil Industry—On the 31st of August, Schimmel & Company, A. G., Miltitz, near Leipzig, Germany, formally celebrated one hundred years of existence, a jubilee which is rare in the essential oil industry.

The firm was founded in the year 1829, on September 1st the name then being Spahn & Büttner. The firm of E. Sachse & Company, Leipzig and their business form was then changed to a limited company (Familien A. G.) In buying this firm they also took over the Sachse branch located in Liesing near Vienna and increased its capacity. In 1929 they bought the firm of Anton Deppe Söhne, located in Hamburg. That is now operated as a branch factory of

Schimmel & Company for the production of such specialties as thymol, borneol, etc. Owing to its favorable location, the Hamburg factory offers special advantages for manufacturing certain products and for export purposes.

In addition to this, the firm also operates a factory in Celje (S. H. S.) and in Budapest, Hungary.

Mr. Karl Fritzsche is chairman of the board of directors and Mr. Hermann Fritzsche is the director, these two constituting the entire board. They have made the name "Schimmel" a hallmark of quality the world over.

The present organization is too well known to make it necessary for us to give space to a description of the many phases of its activities, nor is it necessary to attempt to describe the leading position which the firm occupies in the essential oil and aromatic chemical industry. The scientific part of the establishment has been guided by a number of eminent men, among whom we mention Julius Bertram (1878 to 1900), Carl von Rechenberg (1883 to 1917), Eduard Gildemeister, author of the classical work, "The Volatile Oils," and Heinrich Walbaum, well-known worker in the domain of flower oils and their synthesis. The firm has done a great amount of pioneer work in the chemistry of essential oils and their annual reports are practically textbooks on all up-to-date knowledge of the industry.

We take this opportunity to wish the enterprise and its owners the continued success it so well merits.

STATE ASSOCIATION SECRETARY WANTED—The position of secretary-treasurer of the Pennsylvania Pharmaceutical Association and editor of the *Pennsylvania Pharmacist,* its official publication, has been made vacant by the recent resignation of Mr. J. G. Noh. The Executive Committee desires applications for the position. Applicants should address Mr. J. W. England, chairman of the Executive Committee of the Pennsylvania Pharmaceutical Association, 415 North Thirty-third Street, Philadelphia, giving full information regarding their experience and their qualifications for the work.